PCT







INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY. (PCT)

(51) International Patent Classification ⁷:
C12N 15/12, C07K 14/47, C12Q 1/68,
A61K 39/395, G01N 33/68, 33/574, C07K
16/30, C12N 15/62, 5/02 // A61P 35/00

(11) International Publication Number:

WO 00/04149

(43) International Publication Date:

SN, TD, TG).

27 January 2000 (27.01.00)

(21) International Application Number:

PCT/US99/15838

A2

(22) International Filing Date:

14 July 1999 (14.07.99)

(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

(30) Priority Data:

09/115,453	14 J uly 1998 (14.07.98)	US
09/116,134	14 July 1998 (14.07.98)	US
09/159,822	23 September 1998 (23.09.98)	US
09/159,812	23 September 1998 (23.09.98)	US
09/232,880	15 January 1999 (15.01.99)	US
09/232,149	15 January 1999 (15.01.99)	US
09/288,946	9 April 1999 (09.04.99)	US
·	•	

- (71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).
- (72) Inventors: DILLON, Davin, Clifford; 21607 N.E. 24th Street, Redmond, WA 98053 (US). HARLOCKER, Susan, Louise; 6203 20th Avenue N.W., Seattle, WA 98107 (US). YUQIU, Jiang; 5001 South 232nd Street, Kent, WA 98032 (US). XU, Jiangchun; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). MITCHAM, Jennifer, Lynn; 16677 Northeast 88th Street, Redmond, WA 98052 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE,

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

BNSDOCID: <WO___0004149A2_I_>

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

of America

AM Armenia FI Finland LT Lithuania SK Slovakia AT Austria FR France LU Luxembourg SN Senegal AU Australia GA Gabon LV Latvia SZ Swaziland AZ Azerbaijan GB United Kingdom MC Monaco TD Chad BA Bosnia and Herzegovina GE Georgia MD Republic of Moldova TG Togo BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CA Canada IT Italy MX Mexico UZ Uzbekistan CG Congo KE Kenya NL Netherlands YU Yugoslavia CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CG Compo KE Kenya NL Netherlands CCH Switzerland KR Republic of Korea PL Poland CCN China KR Republic of Korea PL Poland CC Czech Republic LC Saint Lucia RU Russian Federation CC Czech Republic LC Saint Lucia RU Russian Federation CC Cemmany LI Liechtenstein SD Sudan CC Cenmank LK Sri Lanka SE Sweden EE Estonia LI Liberia SG Singapore	AL	Albania	ES	Spain	LS	Lesotho	Sī	Slovenia
AT Austria FR France LU Luxembourg SN Senegal AU Australia GA Gabon LV Latvia SZ Swaziland AZ Azerbaijan GB United Kingdom MC Monaco TD Chad BA Bosnia and Herzegovina GE Georgia MD Republic of Moldova TG Togo BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PL Poland CC Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Demmark LK Sri Lanka SE Sweden	AM	Armenia	FI	Finland	LT			
AU Australia GA Gabon LV Latvia SZ Swaziland AZ Azerbaijan GB United Kingdom MC Monaco TD Chad BA Bosnia and Herzegovina GE Georgia MD Republic of Moldova TG Togo BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BF Burkina Faso IE Ireland MN Mongolia UA Ukraine BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BR Brazil IL Israel MR Mauritania UG Uganda BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CH Switzerland KR Republic of Korea PL Poland CN China KR Republic of Korea PL Poland CC Czech Republic LC Saint Lucia RO Romania CC Czech Republic LC Saint Lucia RO Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	ΑT	Austria	FR	France				
AZ Azerbaijan GB United Kingdom MC Monaco TD Chad BA Bosnia and Herzegovina GE Georgia MD Republic of Moldova TG Togo BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CM Cameroon Republic of Korea PL Poland CM Cameroon Republic of Korea PL Poland CC Cote Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	ΑU	Australia	GA	Gabon		_		•
BA Bosnia and Herzegovina GE Georgia MD Republic of Moldova TG Togo BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CN Cameroon Republic of Korea PL Poland CN Cameroon Republic Of Korea PL Poland CC Cote de Mexico CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	AZ	Azerbaijan	GB	United Kingdom				
BB Barbados GH Ghana MG Madagascar TJ Tajikistan BE Belgium GN Guinea MK The former Yugoslav TM Turkmenistan BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BR Brazil IL Israel MR Mauritania UG Uganda BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PL Poland CC Cz Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BA	Bosnia and Herzegovina	GE					•
BE Belgium GN Guinea MK The former Yugoslav TM Turkey BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CCN China KR Republic of Korea PL Poland CC Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BB	Barbados	GH	•		•		·
BF Burkina Faso GR Greece Republic of Macedonia TR Turkey BG Bulgaria HU Hungary ML Mali TT Trinidad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CM Cameroon Republic of Korea PL Poland CN Cameroon Republic of Korea PL Poland CC Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BE	Belgium	GN	Guinea				-
BG Bulgaria HU Hungary ML Mali TT Triniad and Tobago BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan US United States of Amer CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PL Poland CC Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Enteries Control LK Sri Lanka SE Sweden	BF	Burkina Faso	GR	Greece		•		
BJ Benin IE Ireland MN Mongolia UA Ukraine BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BG	Bulgaria	HU		MI	-		•
BR Brazil IL Israel MR Mauritania UG Uganda BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BJ	Benin	IE				-	
BY Belarus IS Iceland MW Malawi US United States of Amer CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BR	Brazil	IL			_		
CA Canada IT Italy MX Mexico UZ Uzbekistan CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PL Poland CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	BY	Belarus						•
CF Central African Republic JP Japan NE Niger VN Viet Nam CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	CA	Canada						
CG Congo KE Kenya NL Netherlands YU Yugoslavia CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	CF	Central African Republic		•				
CH Switzerland KG Kyrgyzstan NO Norway ZW Zimbabwe CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden	CG	•	-	•		•		
CI Côte d'Ivoire KP Democratic People's NZ New Zealand CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden		_		•			_	•
CM Cameroon Republic of Korea PL Poland CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden						•	zw	Zimbabwe
CN China KR Republic of Korea PT Portugal CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden			123					
CU Cuba KZ Kazakstan RO Romania CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden			KR					
CZ Czech Republic LC Saint Lucia RU Russian Federation DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden								
DE Germany LI Liechtenstein SD Sudan DK Denmark LK Sri Lanka SE Sweden					-	· · · · · · · · · · · · · · · · · · ·		
DK Denmark LK Sri Lanka SE Sweden		-						
PP Estation St Sweden								
SG Singapore								
		Literature	LR	Liocita	SG	Singapore		

COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic

PCT/US99/15838 ··

kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864 SEQ ID NO: 41 is the determined cDNA sequence for P5 SEO ID NO: 42 is the determined cDNA sequence for P8 SEQ ID NO: 43 is the determined cDNA sequence for P9 SEO ID NO: 44 is the determined cDNA sequence for P18 SEO ID NO: 45 is the determined cDNA sequence for P20 SEO ID NO: 46 is the determined cDNA sequence for P29 SEQ ID NO: 47 is the determined cDNA sequence for P30 SEQ ID NO: 48 is the determined cDNA sequence for P34 SEQ ID NO: 49 is the determined cDNA sequence for P36 SEQ ID NO: 50 is the determined cDNA sequence for P38 SEQ ID NO: 51 is the determined cDNA sequence for P39 SEO ID NO: 52 is the determined cDNA sequence for P42 SEQ ID NO: 53 is the determined cDNA sequence for P47 SEQ ID NO: 54 is the determined cDNA sequence for P49 SEQ ID NO: 55 is the determined cDNA sequence for P50 SEQ ID NO: 56 is the determined cDNA sequence for P53 SEO ID NO: 57 is the determined cDNA sequence for P55 SEQ ID NO: 58 is the determined cDNA sequence for P60 SEQ ID NO: 59 is the determined cDNA sequence for P64 SEQ ID NO: 60 is the determined cDNA sequence for P65 SEQ ID NO: 61 is the determined cDNA sequence for P73 SEQ ID NO: 62 is the determined cDNA sequence for P75 SEQ ID NO: 63 is the determined cDNA sequence for P76 SEQ ID NO: 64 is the determined cDNA sequence for P79 SEQ ID NO: 65 is the determined cDNA sequence for P84 SEQ ID NO: 66 is the determined cDNA sequence for P68 SEQ ID NO: 67 is the determined cDNA sequence for P80 SEQ ID NO: 68 is the determined cDNA sequence for P82 SEQ ID NO: 69 is the determined cDNA sequence for U1-3064 SEQ ID NO: 70 is the determined cDNA sequence for U1-3065 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692 SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905 SEQ ID NO: 73 is the determined cDNA sequence for V1-3686 SEQ ID NO: 74 is the determined cDNA sequence for R1-2330 SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736 SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738 SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741 SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734 SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774 SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781 SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785 SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796 SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807 SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810 SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811 SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884 SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896 SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761 SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762 SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770 SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771 SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772 SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297 SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278 SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288 SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283 SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304 SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280 SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S) SEQ ID NO: 108 is the predicted amino acid sequence for F1-12 SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 SEQ ID NO: 115 is the determined cDNA sequence for P89 SEQ ID NO: 116 is the determined cDNA sequence for P90 SEQ ID NO: 117 is the determined cDNA sequence for P92 SEQ ID NO: 118 is the determined cDNA sequence for P95 SEQ ID NO: 119 is the determined cDNA sequence for P98 SEQ ID NO: 120 is the determined cDNA sequence for P102 SEQ ID NO: 121 is the determined cDNA sequence for P110 SEQ ID NO: 122 is the determined cDNA sequence for P111 SEQ ID NO: 123 is the determined cDNA sequence for P114 SEO ID NO: 124 is the determined cDNA sequence for P115 SEQ ID NO: 125 is the determined cDNA sequence for P116 SEQ ID NO: 126 is the determined cDNA sequence for P124 SEQ ID NO: 127 is the determined cDNA sequence for P126 SEQ ID NO: 128 is the determined cDNA sequence for P130 SEQ ID NO: 129 is the determined cDNA sequence for P133 SEQ ID NO: 130 is the determined cDNA sequence for P138 SEQ ID NO: 131 is the determined cDNA sequence for P143 SEQ ID NO: 132 is the determined cDNA sequence for P151 SEQ ID NO: 133 is the determined cDNA sequence for P156 SEQ ID NO: 134 is the determined cDNA sequence for P157 SEQ ID NO: 135 is the determined cDNA sequence for P166 SEQ ID NO: 136 is the determined cDNA sequence for P176 SEQ ID NO: 137 is the determined cDNA sequence for P178 SEQ ID NO: 138 is the determined cDNA sequence for P179 SEQ ID NO: 139 is the determined cDNA sequence for P185 SEQ ID NO: 140 is the determined cDNA sequence for P192 SEQ ID NO: 141 is the determined cDNA sequence for P201 SEQ ID NO: 142 is the determined cDNA sequence for P204 SEQ ID NO: 143 is the determined cDNA sequence for P208 SEQ ID NO: 144 is the determined cDNA sequence for P211 SEQ ID NO: 145 is the determined cDNA sequence for P213 SEQ ID NO: 146 is the determined cDNA sequence for P219 SEQ ID NO: 147 is the determined cDNA sequence for P237 SEQ ID NO: 148 is the determined cDNA sequence for P239 SEQ ID NO: 149 is the determined cDNA sequence for P248

SEQ ID NO: 150 is the determined cDNA sequence for P251 SEQ ID NO: 151 is the determined cDNA sequence for P255 SEQ ID NO: 152 is the determined cDNA sequence for P256 SEQ ID NO: 153 is the determined cDNA sequence for P259 SEQ ID NO: 154 is the determined cDNA sequence for P260 SEQ ID NO: 155 is the determined cDNA sequence for P263 SEQ ID NO: 156 is the determined cDNA sequence for P264 SEQ ID NO: 157 is the determined cDNA sequence for P266 SEQ ID NO: 158 is the determined cDNA sequence for P270 SEQ ID NO: 159 is the determined cDNA sequence for P272 SEQ ID NO: 160 is the determined cDNA sequence for P278 SEQ ID NO: 161 is the determined cDNA sequence for P105 SEQ ID NO: 162 is the determined cDNA sequence for P107 SEQ ID NO: 163 is the determined cDNA sequence for P137 SEQ ID NO: 164 is the determined cDNA sequence for P194 SEQ ID NO: 165 is the determined cDNA sequence for P195 SEQ ID NO: 166 is the determined cDNA sequence for P196 SEQ ID NO: 167 is the determined cDNA sequence for P220 SEQ ID NO: 168 is the determined cDNA sequence for P234 SEQ ID NO: 169 is the determined cDNA sequence for P235 SEQ ID NO: 170 is the determined cDNA sequence for P243 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1 SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1 SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2 SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6 SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13 SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14 SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14 SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-4736 SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-4738 SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-4741 SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-4744 SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-4774 SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-4781 SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785 SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-4787

SEO ID NO: 187 is the determined extended cDNA sequence for 1H-4796 SEO ID NO: 188 is the determined extended cDNA sequence for 1I-4807 SEO ID NO: 189 is the determined 3' cDNA sequence for 1I-4810 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876 SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884 SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896 SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766 SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770 SEO ID NO: 198 is the determined 3' cDNA sequence for 1H-4771 SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772 SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288 SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283 SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304 SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S SEQ ID NO: 225 is the determined cDNA sequence for P703DE5 SEQ ID NO: 226 is the determined cDNA sequence for 9-A11 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6 SEQ ID NO: 228 is the determined cDNA sequence for 8-H7 SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13 SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14 SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24 SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30 SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34 SEQ ID NO: 236 is the determined cDNA sequence for PTPN35 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36 SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39 SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40 SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42 SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46 SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51 SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64 SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67 SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76 SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85 SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87 SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88 SEQ ID NO: 256 is the determined cDNA sequence for JP1F1 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2 SEQ ID NO: 258 is the determined cDNA sequence for JP1C2 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1 SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEO ID NO: 261 is the determined cDNA sequence for JP1D3 SEO ID NO: 262 is the determined cDNA sequence for JP1A4 SEQ ID NO: 263 is the determined cDNA sequence for JP1F5 SEO ID NO: 264 is the determined cDNA sequence for JP1E6 SEQ ID NO: 265 is the determined cDNA sequence for JP1D6 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6 SEQ ID NO: 268 is the determined cDNA sequence for JP1E8 SEO ID NO: 269 is the determined cDNA sequence for JP1D7 SEQ ID NO: 270 is the determined cDNA sequence for JP1D9 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9 SEO ID NO: 273 is the determined cDNA sequence for JP1F12 SEQ ID NO: 274 is the determined cDNA sequence for JP1E12 SEQ ID NO: 275 is the determined cDNA sequence for JP1D11 SEO ID NO: 276 is the determined cDNA sequence for JP1C11 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12 SEQ ID NO: 278 is the determined cDNA sequence for JP1B12 SEO ID NO: 279 is the determined cDNA sequence for JP1A12 SEQ ID NO: 280 is the determined cDNA sequence for JP8G2 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2 SEO ID NO: 283 is the determined cDNA sequence for JP8A3 SEQ ID NO: 284 is the determined cDNA sequence for JP8A4 SEQ ID NO: 285 is the determined cDNA sequence for JP8C3 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6 SEO ID NO: 288 is the determined cDNA sequence for JP8D6 SEO ID NO: 289 is the determined cDNA sequence for JP8F5 SEO ID NO: 290 is the determined cDNA sequence for JP8A8 SEO ID NO: 291 is the determined cDNA sequence for JP8C7 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7 SEQ ID NO: 293 is the determined cDNA sequence for P8D8 SEQ ID NO: 294 is the determined cDNA sequence for JP8E7 SEO ID NO: 295 is the determined cDNA sequence for JP8F8 SEQ ID NO: 296 is the determined cDNA sequence for JP8G8 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

SEQ ID NO: 298 is the determined cDNA sequence for JP8C10 SEQ ID NO: 299 is the determined cDNA sequence for JP8E9 SEQ ID NO: 300 is the determined cDNA sequence for JP8E10 SEQ ID NO: 301 is the determined cDNA sequence for JP8F9 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12 SEQ ID NO: 304 is the determined cDNA sequence for JP8E11 SEQ ID NO: 305 is the determined cDNA sequence for JP8E12 SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12 SEQ ID NO: 307 is the determined cDNA sequence for P711P SEQ ID NO: 308 is the determined cDNA sequence for P712P SEQ ID NO: 309 is the determined cDNA sequence for CLONE23 SEQ ID NO: 310 is the determined cDNA sequence for P774P SEQ ID NO: 311 is the determined cDNA sequence for P775P SEQ ID NO: 312 is the determined cDNA sequence for P715P SEQ ID NO: 313 is the determined cDNA sequence for P710P SEQ ID NO: 314 is the determined cDNA sequence for P767P SEQ ID NO: 315 is the determined cDNA sequence for P768P SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5 SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26 SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23 SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9) SEQ ID NO: 334 is the determined cDNA sequence for P714P SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3) SEQ ID NO: 336 is the predicted amino acid sequence for P705P SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10 SEQ ID NO: 338 is the amino acid sequence of the peptide p5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S SEQ ID NO: 340 is the determined cDNA sequence for P778P

SEQ ID NO: 341 is the determined cDNA sequence for P786P SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984 SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEO ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO:389 is the cDNA sequence for 23379.

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.
SEQ ID NO:415 is the cDNA sequence for 22572.
SEQ ID NO:416 is the cDNA sequence for 22573.
SEQ ID NO:417 is the cDNA sequence for 22573.
SEQ ID NO:418 is the cDNA sequence for 22575.
SEQ ID NO:419 is the cDNA sequence for 22580.
SEQ ID NO:420 is the cDNA sequence for 22581.
SEQ ID NO:421 is the cDNA sequence for 22582.
SEQ ID NO:422 is the cDNA sequence for 22583.
SEQ ID NO:423 is the cDNA sequence for 22584.
SEQ ID NO:424 is the cDNA sequence for 22585.
SEQ ID NO:425 is the cDNA sequence for 22586.
SEQ ID NO:426 is the cDNA sequence for 22587.
SEQ ID NO:427 is the cDNA sequence for 22588.
SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
SEQ ID NO:432 is the cDNA sequence for 22593.
SEQ ID NO:433 is the cDNA sequence for 22594.
SEQ ID NO:434 is the cDNA sequence for 22595.
SEQ ID NO:435 is the cDNA sequence for 22596.
SEQ ID NO:436 is the cDNA sequence for 22847.
SEQ ID NO:437 is the cDNA sequence for 22848.
SEQ ID NO:438 is the cDNA sequence for 22849.
SEQ ID NO:439 is the cDNA sequence for 22851.
SEQ ID NO:440 is the cDNA sequence for 22852.
SEQ ID NO:441 is the cDNA sequence for 22853.
SEQ ID NO:442 is the cDNA sequence for 22854.
SEQ ID NO:443 is the cDNA sequence for 22855.
SEQ ID NO:444 is the cDNA sequence for 22856.
SEQ ID NO:445 is the cDNA sequence for 22857.
SEQ ID NO:446 is the cDNA sequence for 23601.
SEQ ID NO:447 is the cDNA sequence for 23602.
SEQ ID NO:448 is the cDNA sequence for 23605.
SEQ ID NO:449 is the cDNA sequence for 23606.
SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NOs:462-467 are cDNA sequences for known genes.

SEQ ID NOs:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50,

in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to

the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using

standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these

polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothicate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such

as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from

the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (i.e., specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell As used herein, antisera and antibodies are "antigen-specific" if they lines or clones. specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein.

Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are

E. coli, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into

the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from Streptococcus pneumoniae, which synthesizes an N-acetyl-L-alanine amidase known as

amidase LYTA (encoded by the LytA gene; Gene 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of E. coli C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10³ L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from

patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient

time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and

thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (*see also* U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the T cell specificity may be evaluated using any of a variety of standard polypeptide. techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience

(Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4+ or CD8+ T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998,

WO 00/04149

and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or

preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is

quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-

surface receptors or ligands that are not commonly found on dendritic cells in vivo or ex vivo, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., Nature Med. 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that

provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8+ cytotoxic T lymphocytes and CD4+ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein

may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., *Immunological Reviews 157*:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated ex vivo for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such

a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding

agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred

embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4+ and/or CD8+ T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8+ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers

comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the Notl/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with Notl. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/Notl site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64 x 10' independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 106 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of

 H_2O , heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H_2O to form the driver DNA.

To form the tracer DNA, 10 μg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 μl H₂O. Tracer DNA was mixed with 15 μl driver DNA and 20 μl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μl H₂O, mixed with 8 μl driver DNA and 20 μl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human

autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted

amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and

prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4283, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

EXAMPLE 2 DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 $^{\circ}$ C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that

F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression

in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES
BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated

and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable.

Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold overexpression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.

Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following

lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5 FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat norvegicus cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to G. gallus dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

EXAMPLE 6 PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-Ab binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 106 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10⁻⁵ M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of $7\mu g/ml$ dextran sulfate and $25\mu g/ml$ LPS for 3 days). Six days later, cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, Science 258:815-818, 1992) and 3 x 106/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were

restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, J. Immunol., 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 μ g of P1S #10 and 120 μ g of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 μ g/ml P1S#10 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7μ g/ml dextran sulfate and 25μ g/ml LPS for 3 days). Six days later cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10⁶/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly

basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10⁴ cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10⁵ cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed in vitro to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (Critical Reviews in Immunology 18:65-75, 1998). The resulting CD8+ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon ELISPOT assay (see Lalvani et al., J. Exp. Med. 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 104 fibroblasts in the presence of 3 μ g/ml human β_2 -microglobulin and 1 μ g/ml P2S-12 peptide or control E75 In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of y-interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of y-interferon spots with increasing numbers of T

cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 8 PRIMING OF CTL IN VIVO USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

EXAMPLE 9

GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using *in vitro* whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and

priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

EXAMPLE 10 IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis

with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

EXAMPLE 11 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

EXAMPLE 12 ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to

express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxity assays (⁵¹Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med. 186*:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 13 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

69

Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel
		Genes
T-cell gamma chain	P504S	23379 (SEQ
		ID NO:389)
Kallikrein	P1000C	23399 (SEQ
		ID NO:392)
Vector	P501S	23320 (SEQ
		ID NO:386)
CCL 02 PNIA (02210 CFO FF	7.000	
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ
PSA PSA	psies	ID NO:390)
rsa	P510S	
Ald. 6 Dehyd.	P784P	
Ald. O Deliyu.	F/04F	
L-iditol-2 dehydrogenase (23376; SEQ ID	P502S	
NO:388)	13023	
Ets transcription factor PDEF (22672; SEQ	P706P	
ID NO:398)		
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ	
	ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID	
	NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
NO.371)		

transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate

tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was overexpressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

EXAMPLE 14 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA 95*:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

<u>Table II</u>

<u>Prostate cDNA Libraries and ESTs</u>

Frontie CDIVA Citialies and ESTS				
Library	# of Libraries	# of ESTs		
Plus	25	43,482		
Normal	11	18,875		
Tumor	11	21,769		
Cell lines	3	2,838		
Minus	166			
Other	287			

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

<u>Table III</u> <u>Prostate Cluster Summary</u>

	Trostate Craster Summary				
		# of	# of ESTs		
7	Гуре	Superclusters	Ordered		
1		688	677		
2		2899	2484		
3		. 85	11		
4		673	0		
	Total	4345	3172		

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

<u>Table IV</u> <u>Prostate-tumor Specific Clones</u>

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P

400		
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

22851	PAP
22852	PAP
22853	PAP
22854	previously identified P509S
22855	previously identified P705P
22856	previously identified P774P
22857	PSA
23601	previously identified P777P
23602	PSA
23605	PSA
23606	PSA
23612	novel
23614	PSA
23618	previously identified P1000C
23622	previously identified P705P
	22852 22853 22854 22855 22856 22857 23601 23602 23605 23606 23612 23614 23618

EXAMPLE 15 FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

EXAMPLE 16 FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

- 1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;
- (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and
 - (c) complements of any of the sequence of (a) or (b).
- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.
- 3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.
- 4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

78

435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

- 5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
- 9. An expression vector comprising a polynucleotide according to any one of claims 4-7.
- 10. A host cell transformed or transfected with an expression vector according to claim 9.
 - 11. An expression vector comprising a polynucleotide according claim 8.

- 12. A host cell transformed or transfected with an expression vector according to claim 11.
- 13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.
- 16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.
- 18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.
- 19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.
- 20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

- 22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.
- 23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.
- 24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.
- 27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.
- 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.
- 31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

- 32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.
- 34. A method according to any one of claims 29-32, wherein the cancer is prostate cancer.
- 35. A fusion protein comprising at least one polypeptide according to claim 1.
- 36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.
- 39. An isolated polynucleotide encoding a fusion protein according to claim 35.
- 40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.
- 41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.
- 42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

- 43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.
- 45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.
- 46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.
- 47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.
- 49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.
- 50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
 - (ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.

- 52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.
- 53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii); under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- 54. An isolated T cell population, comprising T cells prepared according to the method of claim 53.
- 55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.
- 56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

- 57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.
- 58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 59. A method according to claim 58, wherein the binding agent is an antibody.
- 60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

- 61. A method according to claim 58, wherein the cancer is prostate cancer.
- 62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 63. A method according to claim 62, wherein the binding agent is an antibody.
- 64. A method according to claim 63, wherein the antibody is a monoclonal antibody.
- 65. A method according to claim 62, wherein the cancer is a prostate cancer.
- 66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
 - 72. A diagnostic kit, comprising:
 - (a) one or more antibodies according to claim 21; and
 - (b) a detection reagent comprising a reporter group.

- 73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.
- 74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
- 77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.
- 78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
 - 79. A diagnostic kit, comprising:
 - (a) an oligonucleotide according to claim 77; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

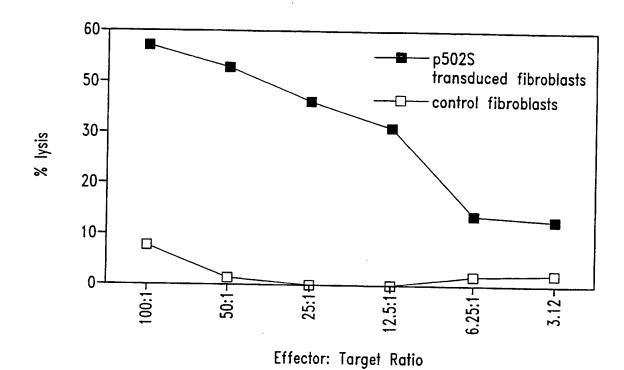


Fig. 1

1.

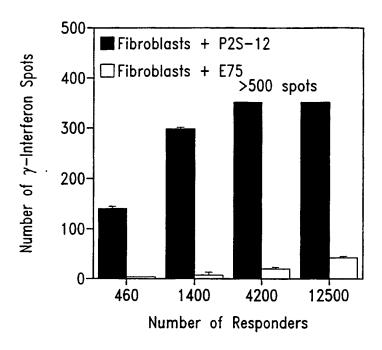


Fig. 2A

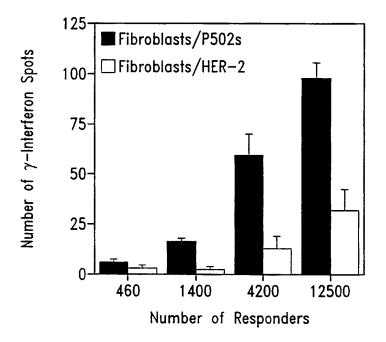
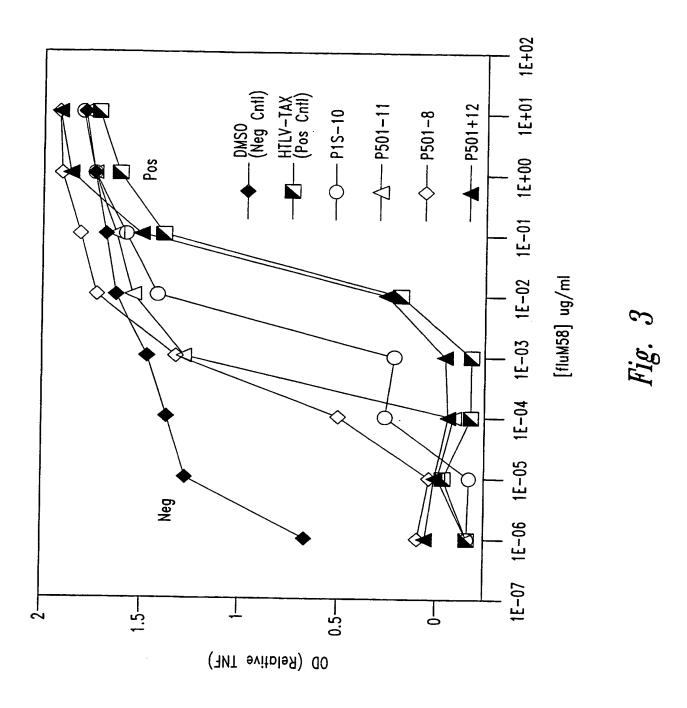


Fig. 2B

SUBSTITUTE SHEET (RULE 26)

1



SUBSTITUTE SHEET (RULE 26)

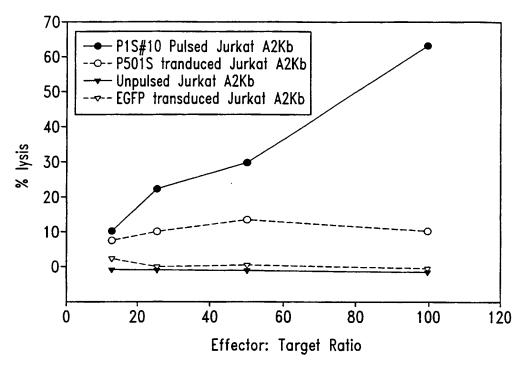
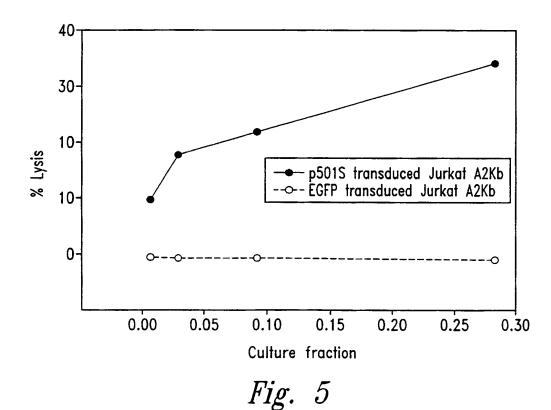
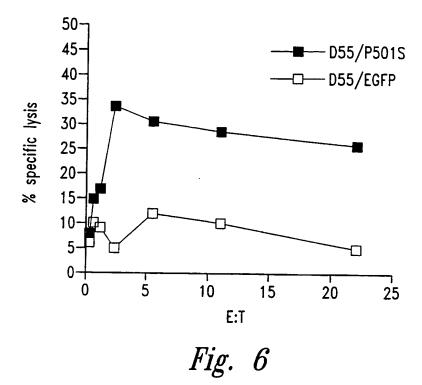
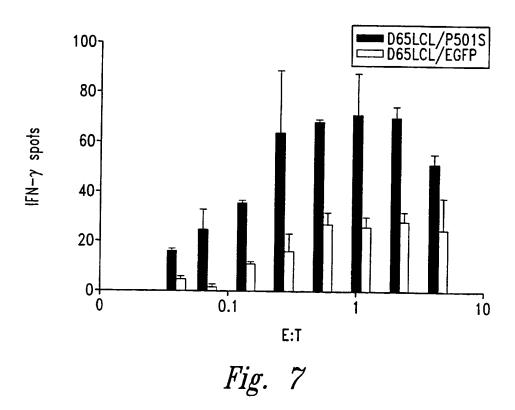


Fig. 4



SUBSTITUTE SHEET (RULE 26)





SEQUENCE LISTING

```
<110> Corixa Corporation
      <120> COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS
        OF PROSTATE CANCER AND METHODS FOR THEIR USE
      <130> 210121.42701PC
      <140> PCT
      <141> 1999-07-08
      <160> 472
      <170> FastSEQ for Windows Version 3.0
      <210> 1
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(814)
      <223> n = A,T,C or G
      <400> 1
ttttttttt tttttcacag tataacagct ctttatttct gtgagttcta ctaggaaatc
                                                                        60
atcaaatctg agggttgtct ggaggacttc aatacacctc cccccatagt gaatcagctt
                                                                       120
ccaqqqqqtc caqtccctct ccttacttca tccccatccc atgccaaagg aaqacctcc
                                                                       180
ctccttggct cacagcette tetaggette ccagtgeete caggacagag tgggttatgt
                                                                       240
tttcagctcc atccttgctg tgagtgtctg gtgcgttgtg cctccagctt ctgctcagtg
                                                                       300
cttcatggac agtgtccagc acatgtcact ctccactctc tcagtgtgga tccactagtt
                                                                       360
ctagagcggc cgccaccgcg gtggagctcc agcttttgtt ccctttagtg agggttaatt
                                                                       420
gcgcgcttgg cgtaatcatg gtcataactg tttcctgtgt gaaattgtta tccgctcaca
                                                                       480
attccacaca acatacgagc cggaagcata aagtgtaaag cctggggtgc ctaatgagtg
                                                                       540
anctaactca cattaattgc gttgcgctca ctgnccgctt tccagtcngg aaaactgtcg
                                                                       600
tgccagctgc attaatgaat cggccaacgc ncggggaaaa gcggtttgcg ttttgggggc
                                                                       660
tetteegett etegeteaet nanteetgeg eteggtentt eggetgeggg gaacggtate
                                                                       720
actcctcaaa ggnggtatta cggttatccn naaatcnggg gatacccngg aaaaaanttt
                                                                       780
aacaaaaggg cancaaaggg cngaaacgta aaaa
                                                                       814
      <210> 2
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(816)
      <223> n = A,T,C or G
      <400> 2
acagaaatgt tggatggtgg agcacctttc tatacgactt acaggacagc agatggggaa
                                                                        60
ttcatggctg ttggagcaat agaaccccag ttctacgagc tgctgatcaa aggactfgga
                                                                       120
```

```
ctaaagtctg atgaacttcc caatcagatg agcatggatg attggccaga aatgaagaag
                                                                        180
aagtttgcag atgtatttgc aaagaagacg aaggcagagt ggtgtcaaat ctttgacggc
                                                                        240
acagatgcct gtgtgactcc ggttctgact tttgaggagg ttgttcatca tgatcacaac
                                                                        300
aaggaacggg gctcgtttat caccagtgag gagcaggacg tgagcccccg ccctgcacct
                                                                        360
ctgctgttaa acaccccagc catcccttct ttcaaaaggg atccactagt tctagaagcg
                                                                        420
gccgccaccg cggtggagct ccagcttttg ttccctttag tgagggttaa ttgcgcgctt
                                                                        480
ggcgtaatca tggtcatagc tgtttcctgt gtgaaattgt tatccgctca caattccccc
                                                                        540
aacatacgag ccggaacata aagtgttaag cctggggtgc ctaatgantg agctaactcn
                                                                        600
cattaattgc gttgcgctca ctgcccgctt tccagtcggg aaaactgtcg tgccactgcn
                                                                        660
ttantgaatc ngccacccc cgggaaaagg cggttgcntt ttgggcctct tccgctttcc
                                                                        720
tegeteattg atcetngene eeggtetteg getgeggnga aeggtteaet ceteaaagge
                                                                        780
ggtntnccgg ttatccccaa acnggggata cccnga
                                                                        816
      <210> 3
      <211> 773
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (773)
      <223> n = A,T,C or G
      <400> 3
cttttgaaag aagggatggc tggggtgttt aacagcagag gtgcagggcg ggggctcacg
                                                                        60
tectgetect caetggtgat aaacgagece egtteettgt tgtgateatg atgaacaace
                                                                        120
tecteaaaag teagaacegg agteacaeag geatetgtge egteaaagat ttgacaecae
                                                                        180
tetgeetteg tettetttge aaatacatet geaaaettet tetteattte tggeeaatea
                                                                        240
tecatgetea tetgattggg aagtteatea gaetttagte cannteettt gateageage
                                                                        300
tegtagaact ggggttetat tgetecaaca gecatgaatt eeccatetge tgteetgtaa
                                                                       360
gtcgtataga aaggtgctcc accatccaac atgttctgtc ctcgaggggg ggcccggtac
                                                                       420
ccaattcgcc ctatantgag tcgtattacg cgcgctcact ggccgtcgtt ttacaacgtc
                                                                       480
gtgactggga aaaccctggg cgttaccaac ttaatcgcct tgcagcacat ccccctttcg
                                                                       540
ccagctgggc gtaatancga aaaggcccgc accgatcgcc cttccaacag ttgcgcacct
                                                                       600
gaatgggnaa atgggacccc cctgttaccg cgcattnaac ccccgcnggg tttngttgtt
                                                                       660
acceccaent nnacegetta caetttgeca gegeettane gecegeteee ttteneettt
                                                                       720
cttcccttcc tttcncnccn ctttcccccg gggtttcccc cntcaaaccc cna
                                                                       773
      <210> 4
      <211> 828
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(828)
      <223> n = A, T, C or G
      <400> 4
cctcctgagt cctactgacc tgtgctttct ggtgtggagt ccagggctgc taggaaaagg
                                                                        60
aatgggcaga cacaggtgta tgccaatgtt tctgaaatgg gtataatttc gtcctctcct
                                                                       120
teggaacact ggctgtetet gaagaettet egeteagttt eagtgaggae acacacaaag
                                                                       180
acgtgggtga ccatgttgtt tgtggggtgc agagatggga ggggtggggc ccaccctgga
                                                                       240
agagtggaca gtgacacaag gtggacactc tctacagatc actgaggata agctggagcc
                                                                       300
acaatgcatg aggcacacac acagcaagga tgacnctgta aacatagccc acgctgtcct
                                                                       360
```

540

```
qnqqqcactg ggaagcctan atnaggccgt gagcanaaag aaggggagga tccactagtt
                                                                       420
ctanagegge egecacegeg gtgganetee anettttgtt ecetttagtg agggttaatt
                                                                       480
qcqcqcttgg cntaatcatg gtcatanctn tttcctgtgt gaaattgtta tccgctcaca
                                                                       540
attccacaca acatacganc cggaaacata aantgtaaac ctggggtgcc taatgantga
                                                                       600
ctaactcaca ttaattgcgt tgcgctcact gcccgctttc caatcnggaa acctgtcttg
                                                                       660
concettgeat that gaaten gecaaceee ggggaaaage gettgegetet tgggegetet
                                                                       720
teegetteet eneteantta nteeetnene teggteatte eggetgenge aaaceggtte
                                                                       780
accnecteda aagggggtat teeggtttee cenaateegg ggananee
                                                                       828
      <210> 5
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 5
ttttttttt tttttactga tagatggaat ttattaaget tttcacatgt gatagcacat
                                                                        60
                                                                       120
agttttaatt gcatccaaag tactaacaaa aactctagca atcaagaatg gcagcatgtt
attttataac aatcaacacc tgtggctttt aaaatttggt tttcataaga taatttatac
                                                                       180
tgaagtaaat ctagccatgc ttttaaaaaa tgctttaggt cactccaagc ttggcagtta
                                                                       240
acatttggca taaacaataa taaaacaatc acaatttaat aaataacaaa tacaacattg
                                                                       300
taggccataa tcatatacag tataaggaaa aggtggtagt gttgagtaag cagttattag
                                                                       360
aataqaatac cttggcctct atgcaaatat gtctagacac tttgattcac tcagccctga
                                                                       420
                                                                       480
cattcagttt tcaaagtagg agacaggttc tacagtatca ttttacagtt tccaacacat
tgaaaacaag tagaaaatga tgagttgatt tttattaatg cattacatcc tcaagagtta
                                                                       540
tcaccaaccc ctcagttata aaaaattttc aagttatatt agtcatataa cttggtgtgc
                                                                       600
                                                                       660
ttattttaaa ttagtgctaa atggattaag tgaagacaac aatggtcccc taatgtgatt
gatattggtc atttttacca gcttctaaat ctnaactttc aggcttttga actggaacat
                                                                       720
                                                                       780
tqnatnacag tgttccanag ttncaaccta ctggaacatt acagtgtgct tgattcaaaa
                                                                       834
tqttattttg ttaaaaatta aattttaacc tggtggaaaa ataatttgaa atna
      <210> 6
      <211> 818
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(818)
      \langle 223 \rangle n = A,T,C or G
      <400> 6
                                                                        60
ttttttttt tttttttt aagaccctca tcaatagatg gagacataca gaaatagtca
aaccacatct acaaaatgcc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga
                                                                        120
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagttg agccaataat
                                                                        180
                                                                        240
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcgga
aatggtgaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagacccag
                                                                        300
                                                                        360
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgttttcta ttagactatg
                                                                        420
gtgagctcag gtgattgata ctcctgatgc gagtaatacg gatgtgttta ggagtgggac
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgccctccta gttggggggt
                                                                        480
```

aggggctagg ctggagtggt aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga

```
ggtaataaat aggattatcc cgtatcgaag gcctttttgg acaggtggtg tgtggtgcc
                                                                        600
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgttggg
                                                                        660
ttantangge ctantatgaa gaacttttgg antggaatta aatcaatnge ttggeeggaa
                                                                        720
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta cccnacccat
                                                                        780
ggaatnence ecceggaena ntgnatecet attettaa
                                                                        818
      <210> 7
      <211> 817
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(817)
      \langle 223 \rangle n = A,T,C or G
      <400> 7
ttttttttt tttttttt tggctctaga gggggtagag ggggtgctat agggtaaata
                                                                        60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt
                                                                       120
ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcggtga
                                                                       180
aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaat gtggggacag
                                                                       240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga
                                                                       300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg
                                                                       360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc
                                                                       420
attggtggcc aattgatttg atggtaaggg gagggatcgt tgaactcgtc tgttatgtaa
                                                                       480
aggatneett ngggatggga aggenatnaa ggaetangga tnaatggegg geangatatt
                                                                       540
tcaaacngtc tctanttcct gaaacgtctg aaatgttaat aanaattaan tttngttatt
                                                                       600
gaatnttnng gaaaagggct tacaggacta gaaaccaaat angaaaanta atnntaangg
                                                                       660
cnttatentn aaaggtnata accnetecta tnateceace caatngnatt ecceaenenn
                                                                       720
acnattggat nececantte canaaangge enececegg tgnanneene ettttgttee
                                                                       780
cttnantgan ggttattcnc ccctngcntt atcancc
                                                                       817
      <210> 8
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(799)
      <223> n = A,T,C or G
      <400> 8
catttccggg tttactttct aaggaaagcc gagcggaagc tgctaacgtg ggaatcggtg
                                                                        60
cataaggaga actitctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt
                                                                       120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag
                                                                       180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg
                                                                       240
tgggtggccg angectgane egetetgeet tgetgeece angtgggeeg ecaceceetg
                                                                       300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac ccccacangg
                                                                       360
ggattttgct cctanantaa ggctcatctg ggcctcggcc ccccacctg gttggccttg
                                                                       420
tetttgangt gageeceatg teeatetggg ceaetgteng gaceaecttt ngggagtgtt
                                                                       480
ctccttacaa ccacannatg cccggctcct cccggaaacc antcccancc tgngaaggat
                                                                       540
caagneetgn atccactnnt netanaaccg geenceneeg engtggaacc encettntgt
                                                                       600
teetttent tnagggttaa tnnegeettg geettneean ngteetnene ntttteennt
                                                                       660
gttnaaattg ttangeneee neennteeen ennennenan eeegaeeenn annttnnann
                                                                       720
```

```
ncctqqqqt nccnncqat tgacccnncc ncctntant tgcnttnggg nncnntgccc
                                                                       780
                                                                       799
ctttccctct nggganncg
      <210> 9
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A, T, C or G
      <400> 9
                                                                        60
acqccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtggtttg
taanqatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct
                                                                       120
caaqqacaag gccaccaggt gcgggggccg aagcccacat gatccttact ctatgagcaa
                                                                       180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccanq
                                                                       240
caggicatgg ggitgingnc caactggggg ccncaacgca aaanggcnca gggccicngn
                                                                       300
cacccatccc angacgeggc tacactnetg gacetecene tecaccaett teatgegetg
                                                                       360
ttentaceeg egnatnigte ceaneigtit engigeenae tecaneitet nggaegigeg
                                                                       420
ctacatacge eeggantene netecegett tgteectate eaegtneean eaacaaattt
                                                                       480
                                                                       540
cncentantg cacenattee caentttnne agnttteene nnegngette ettntaaaag
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn ccccctnata
                                                                       600
gctgaantcc ccatnaccnn gnctcnatgg ancenteent tttaannaen ttetnaactt
                                                                       660
gggaanance etegneentn ecceenttaa teceneettg enangnnent ecceenntee
                                                                       720
necennntng gentntnann enaaaaagge eennnaneaa teteetnnen eeteantteg
                                                                       780
ccancecteg aaateggeen e
                                                                       801
      <210> 10
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
      \langle 223 \rangle n = A,T,C or G
      <400> 10
cagtetaint ggeeagigig geagetitee eigiggeige eggigeeaea igeeigieee
                                                                        60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc
                                                                        120
agatectgee etacacactg gesteestet accaceggga gaagcaggtg tteetgessa
                                                                        180
                                                                       240
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc
caggecetaa geetggaget eeetteeeta atggacaegt gggtgetgga ggeagtggee
                                                                        300
tgctcccacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg
                                                                        360
tggtgggtga gcccaccgan gccagggtgg ttccgggccg gggcatctgc ctggacctcg
                                                                        420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat
                                                                        480
tgtccagctc agccagtctg tcactgccta tatggtgtct gccgcaggcc tgggtctggt
                                                                        540
                                                                        600
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg
                                                                        660
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc
                                                                        720
tectgttaac eccatgggge tgeeggettg geegecaatt tetgttgetg ecaaantnat
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng
                                                                        780
                                                                        789
ggngttccc
```

```
<210> 11
       <211> 772
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(772)
       <223> n = A,T,C or G
       <400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac
                                                                         60
tttgttaaat aaataagtta aatatttaaa tgcctgtgtc tctgtgatgg caacagaagg
                                                                        120
accaacaggc cacatcctga taaaaggtaa gagggggtg gatcagcaaa aagacagtgc
                                                                        180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata
                                                                        240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag
                                                                        300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt
                                                                        360
tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc
                                                                        420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc
                                                                        480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana
                                                                        540
aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca
                                                                        600
gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca
                                                                        660
accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca
                                                                        720
ggcccnccac cccnaatntt gctgggaaat ttttcctccc ctaaattntt tc
                                                                        772
      <210> 12
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(751)
      \langle 223 \rangle n = A,T,C or G
      <400> 12
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                         60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca
                                                                       300
ggcactacca gcaacgtcag ggaagtgctc agccattgtg gtgtacacca aggcgaccac
                                                                       360
agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc
                                                                       420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna
                                                                       480
cnccggctgc gatgaagaaa tnaccccncg ttgacaaact tgcatggcac tggganccac
                                                                       540
agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg
                                                                       600
ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct
                                                                       660
tnatnaacnt gaaccetgen tngtggetee tgtteaggne ennggeetga ettetnaann
                                                                       720
aangaacton gaagnoocca enggananne g
                                                                       751
      <210> 13
      <211> 729
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(729)
      <223> n = A,T,C or G
      <400> 13
gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgtcctt
                                                                         60
tgtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc
                                                                        120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt
                                                                        180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt
                                                                        240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc
                                                                        300
ctcatcqcaq ccggcgttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag
                                                                        360
actgagagea agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct
                                                                        420
                                                                        480
gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt
                                                                        540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt
                                                                        600
gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa
                                                                        660
acgtccccaa cacagccaat tgaaaacctg cacccaaccc aaangggtcc ccaaccanaa
                                                                        720
                                                                        729
attnaaggg
      <210> 14
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(816)
      \langle 223 \rangle n = A,T,C or G
      <400> 14
tgctcttcct caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgcag
                                                                         60
                                                                        120
tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct
ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag
                                                                        180
ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt gggggtgtct
                                                                        240
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga
                                                                        300
cangtgccag agcacactgg atggcgcctt tccatgnnan gggccctgng ggaaagtccc
                                                                        360
tganccccan anctgcctct caaangcccc accttgcaca ccccgacagg ctagaatgga
                                                                        420
atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt
                                                                        480
gcanatetge teegnggggg tentantace ancgtgggaa aagaaceeca ggengegaac
                                                                        540
caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna
                                                                        600
ctgtnnanct ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact
                                                                        660
gggacaaggt aantngcent cetttnaatt ecenanentn eeeeetggtt tggggttttn
                                                                        720
cncnctccta ccccagaaan nccgtgttcc cccccaacta ggggccnaaa ccnnttnttc
                                                                        780
cacaaccctn ccccacccac gggttcngnt ggttng
                                                                        816
      <210> 15
      <211> 783
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(783)
      \langle 223 \rangle n = A,T,C or G
```

```
<400> 15
ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg
                                                                         60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagaga
                                                                        120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga
                                                                        180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca
                                                                        240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt
                                                                        300
tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggaggct
                                                                        360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcngggtg
                                                                        420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct
                                                                        480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca
                                                                        540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa
                                                                        600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccgg
                                                                        660
cncctccntt ttccccnntn aacaaagggc nctngcnttt gaactgcccn aacccnggaa
                                                                        720
tetneenngg aaaaantnee eeceetggtt eetnnaanee eeteenenaa anetneeeee
                                                                       780
CCC
                                                                        783
      <210> 16
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A,T,C or G
      <400> 16
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtagggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca
                                                                       300
ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcgaccaca
                                                                       360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca
                                                                       420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg
                                                                       480
ccngctgcga atgaaagaaa ntacccacgt tgacaaactg catggccact ggacgacagt
                                                                       540
tggcccgaan atcttcagaa aagggatgcc ccatcgattg aacacccana tgcccactgc
                                                                       600
cnacaggget geneenenen gaaagaatga geeattgaag aaggatente ntggtettaa
                                                                       660
tgaactgaaa centgeatgg tggeeeetgt teagggetet tggeagtgaa ttetganaaa
                                                                       720
aaggaacngc ntnagccccc ccaaangana aaacaccccc gggtgttgcc ctgaattggc
                                                                       780
ggccaaggan ccctgccccn g
                                                                       801
      <210> 17
      <211> 740
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(740)
      <223> n = A, T, C or G
      <400> 17
gtgagagcca ggcgtccctc tgcctgccca ctcagtggca acacccggga gctgttttgt
```

```
cetttgtgga geetcageag tteeetettt cagaacteae tgecaagage cetgaacagg
                                                                        120
agccaccatg cagtgettea getteattaa gaccatgatg atcetettea atttgeteat
                                                                        180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc
                                                                        240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta
                                                                        300
cttcctcatc gcagccggcg ttgtggtctt tgctcttggt ttcctgggct gctatggtgc
                                                                        360
taagacggag agcaagtgtg ceetegtgae gttettette ateeteetee teatetteat
                                                                        420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct
                                                                        480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc
                                                                        540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg
                                                                        600
gaattttgaa aganteneee taetteeaaa aaaaaanant tgeetttnee eeenttetgt
                                                                        660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa
                                                                        720
caaaaaant nnaagggttn
                                                                        740
      <210> 18
      <211> 802
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(802)
      \langle 223 \rangle n = A,T,C or G
      <400> 18
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca
                                                                         60
caaggtette cagetgeege acattaegea gggeaagage etceageaac actgeatatq
                                                                        120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct
                                                                        180
gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat
                                                                        240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa
                                                                        300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat
                                                                        360
ggatgagtgt ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct
                                                                        420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg
                                                                       480
gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc
                                                                       540
gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cnctacttgc
                                                                       600
aancttcgtc nggcccatgg aattcaccnc accggaactn gtangatcca ctnnttctat
                                                                       660
aaccggncgc caccgcnnnt ggaactccac tettnttnee tttaettgag ggttaaggte
                                                                       720
accettnneg ttacettggt ceaaacentn centgtgteg anatngtnaa tenggneena
                                                                       780
tnccancene atangaagee ng
                                                                       802
      <210> 19
      <211> 731
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(731)
      <223> n = A,T,C or G
      <400> 19
cnaagettee aggtnaeggg eegenaance tgaeeenagg tancanaang eagnengegg
                                                                        60
gagcccaccg tcacgnggng gngtctttat nggaggggc ggagccacat cnctggacnt
                                                                       120
entgacecca acteceence neneantgea gtgatgagtg cagaactgaa ggtnacgtgg
                                                                       180
caggaaccaa gancaaanne tgeteennte caagteggen nagggggegg ggetggecae
                                                                       240
geneateent enagtgetgn aaageeeenn eetgtetaet tgtttggaga aengennnga
                                                                       300
```

```
catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcgcan
                                                                        360
cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaatc tnccncccct
                                                                        420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta
                                                                        480
aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg
                                                                        540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc
                                                                        600
cnncnntcca aggggggnc ggccccaat cccccaacc ntnaattnan tttancccn
                                                                        660
cccccnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac
                                                                        720
nnaatccncc t
                                                                        731
      <210> 20
      <211> 754
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(754)
      \langle 223 \rangle n = A,T,C or G
      <400> 20
ttttttttt tttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc
                                                                        60
caaccccctc ntccaaatnn ccntttccgg gngggggttc caaacccaan ttanntttgg
                                                                       120
annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta
                                                                       180
tnancttnaa tncctggaaa congtngntt ccaaaaatnt ttaaccctta antocctccg
                                                                       240
aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc
                                                                       300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa
                                                                       360
ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg
                                                                       420
ganccenegg gaattaacgg ggnnnnteee tnttgggggg enggnneece eccenteggg
                                                                       480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc
                                                                       540
ccaggntgag nntngggttt ncccccccc canggcccct ctcgnanagt tggggtttgg
                                                                       600
ggggcctggg attituttic ccctnttncc tcccccccc ccnggganag aggttngngt
                                                                       660
tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga
                                                                       720
agtccnttgn agggntaaan ggccccctnn cqqq
                                                                       754
      <210> 21
      <211> 755
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(755)
      <223> n = A,T,C or G
      <400> 21
atcaneccat gacecenaac nngggacene teaneeggne nnnenacene eggeenatea
                                                                        60
nngtnagnne actnennttn nateaeneee encenaetae geeenenane enaegeneta
                                                                       120
nncanatnee actganngeg egangtngan ngagaaanet nataccanag neaccanaen
                                                                       180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn
                                                                       240
nnenneanat gatttteetn ancegattae centneecce tancecetee ecceeaacna
                                                                       300
cgaaggenet ggneenaagg nngegnenee cegetagnte ecenneaagt eneneneeta
                                                                       360
aactcancen nattaenege ttentgagta teacteeceg aateteacee tacteaacte
                                                                       420
aaaaanatcn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt
                                                                       480
ttagnggtcc ntnaanchtc ctaatacttc cagtctncct tcnccaattt ccnaanggct
                                                                       540
ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttcntngaac
                                                                       600
```

```
gggctcntct tttccttcgg ttancctggn ttcnnccggc cagttattat ttcccntttt
                                                                       660
aaattentne entttanttt tggenttena aaceeegge ettgaaaaeg geeecetggt
                                                                       720
aaaaggttgt tttganaaaa tttttgtttt gttcc
                                                                       755
      <210> 22
      <211> 849
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(849)
      \langle 223 \rangle n = A,T,C or G
      <400> 22
ttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt
                                                                        60
acgctnggan taangcgacc cganttctag gannencect aaaatcanac tgtgaagatn
                                                                       120
atectgnnna eggaanggte aceggnngat nntgetaggg tgncenetee cannnenttn
                                                                       180
cataacteng nggeeetgee caccacette ggeggeeeng ngneegggee egggteattn
                                                                       240
gnnttaaccn cactnigena neggttteen neecenneng accenggega teeggggtne
                                                                       300
totqtottoo cotgnagnon anaaantggg conoggnooc otttaccoot nnacaagooa
                                                                       360
engeenteta neenengeee eeceteeant nngggggaet geenannget eegttnetng
                                                                       420
nnaccccnnn gggtncctcg gttgtcgant cnaccgnang ccanggattc cnaaggaagg
                                                                       480
tgcgttnttg gcccctaccc ttcgctncgg nncacccttc ccgacnanga nccgctcccg
                                                                       540
enennegning cetenecteg caacacege netentengt neggninece ecceacege
                                                                       600
necetenene ngnegnanen eteeneenee gteteannea ceaeceegee eegeeaqgee
                                                                       660
ntcanccacn ggnngacnng nagcnennte geneegegen gegneneeet egeenengaa
                                                                       720
ctncntcngg ccantnncgc tcaanccnna cnaaacgccg ctgcgcggcc cgnagcgncc
                                                                       780
necteenega gteeteeegn etteenaeee angnntteen egaggaeaen nnaeeeegee
                                                                       840
                                                                       849
nncangcgg
      <210> 23
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(872)
      <223> n = A,T,C or G
      <400> 23
gegeaaacta tacttegete gnactegtge geetegetne tetttteete egeaaceatg
                                                                        60
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca
                                                                       120
cacaenenan aganaaatee netgeettee anagtanaen attgaaenng agaaecange
                                                                       180
nggegaateg taatnaggeg tgegeegeea atntgtenee gtttattntn ceagentene
                                                                       240
ctnccnaccc tacntcttcn nagctgtcnn acccctngtn cgnacccccc naggtcggga
                                                                       300
tegggtttnn nntgacegng enneceetee eccenteeat naeganeene eegeaceaee
                                                                       360
nanngenege neceegnnet ettegeenee etgteetntn eecetgtnge etggenengn
                                                                       420
accgcattga ccctcgccnn ctncnngaaa ncgnanacgt ccgggttgnn annancgctg
                                                                       480
tgggnnngcg tetgeneege gtteetteen nennetteea ceatettent taengggtet
                                                                       540
conceptate tennacean cotegeace thicotate coccettae tecceccett
                                                                       600
cgncgtgncc cgnccccacc ntcatttnca nacgntcttc acaannncct ggntnnctcc
                                                                       660
                                                                       720
cnancingnen gtcancenag ggaagggngg ggnneenntg nttgaegttg nggngangte
                                                                       780
cgaanantcc tencentean enctaceeet egggegnnet etengttnee aacttaneaa
```

WO 00/04149

```
ntctcccccg ngngcncntc tcagcctcnc ccnccccnct ctctgcantg tnctctgctc
                                                                        840
 tnaccnntac gantnttcgn cnccctcttt cc
                                                                        872
       <210> 24
       <211> 815
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(815)
       <223> n = A,T,C or G
       <400> 24
gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggtcnta
                                                                         60
nctgncttcc tgtgtcaaat gtatacnaan tanatatgaa tctnatntga caaganngta
                                                                        120
tentneatta gtaacaantg tnntgteeat eetgtengan canatteeca tnnattnegn
                                                                        180
cgcattenen geneantatn taatngggaa ntennntnnn neacenneat etatentnee
                                                                        240
geneeetgae tggnagagat ggatnantte tnntntgace nacatgttea tettggattn
                                                                        300
aananccccc cgcngnccac cggttngnng cnagccnntc ccaagacctc ctgtggaggt
                                                                        360
aacctgcgtc aganncatca aacntgggaa acccgcnncc angtnnaagt ngnnncanan
                                                                        420
gatcccgtcc aggnttnacc atcccttcnc agcgccccct ttngtgcctt anagngnagc
                                                                        480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc
                                                                        540
gaacccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccncanc
                                                                        600
cccnccctac ccnnctttgg gacngtgacc aanteccgga gtnccagtcc ggccngncte
                                                                       660
ccccaccggt nnccntgggg gggtgaanct cngnntcanc cngncgaggn ntcgnaagga
                                                                       720
accggneetn ggnegaanng anenntenga agngeenent egtataacce eccetencea
                                                                       780
ncenaengnt agnteecece engggtnegg aangg
                                                                       815
      <210> 25
      <211> 775
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(775)
      <223> n = A,T,C or G
      <400> 25
ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct actctcttt tctggcctgg
                                                                        60
aggctatcca gcgtactcca aagattcagg tttactcacg tcatccagca gagaatggaa
                                                                       120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact
                                                                       180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg
                                                                       240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg
                                                                       300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca
                                                                       360
tgtaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt
                                                                       420
ctgcttgctt gcnttttaat antgatatgc ntatacaccc taccctttat gnccccaaat
                                                                       480
tgtaggggtt acatnantgt tcncntngga catgatcttc ctttataant ccnccnttcg
                                                                       540
aattgcccgt enccengttn ngaatgttte ennaaceaeg gttggeteee ecaggtenee
                                                                       600
tcttacggaa gggcctgggc cnctttncaa ggttggggga accnaaaatt tcncttntgc
                                                                       660
concoencea ennicitigng nnoncantit ggaaccette enatteeest tggestenna
                                                                       720
nccttnncta anaaaacttn aaancgtngc naaanntttn acttcccccc ttacc
                                                                       775
```

<210> 26

```
<211> 820
             <212> DNA
             <213> Homo sapien
             <220>
             <221> misc feature
             <222> (1)...(820)
             <223> n = A,T,C or G
             <400> 26
 anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat
                                                                                                                                            60
 cccanagata ncttatanca acagtgcttt gaccaagagc tgctgggcac atttcctgca
                                                                                                                                          120
 gaaaaggtgg cggtccccat cactcctcct ctcccatagc catcccagag gggtgagtag
                                                                                                                                          180
 ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca
                                                                                                                                          240
 ntqatqacca tgggcgggag cgagcctctt ccctgnaccg gggtggcana nganagccta
                                                                                                                                          300
 nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc
                                                                                                                                          360
 ttcctacctq acnaccagng accnnnaact gcngcctggg gacagcnctg ggancagcta
                                                                                                                                          420
                                                                                                                                          480
 acnnageact cacetgeece eccatggeeg thegenteec tggteetgne aagggaaget
 ccctqttqqa attncqqqqa naccaaggga nccccctcct ccanctgtga aggaaaaann
                                                                                                                                          540
 gatggaattt tncccttccg gccnntcccc tcttccttta cacgccccct nntactcntc
                                                                                                                                          600
 tecetetntt nteetquene aettttnace cennuattte eettnattga teggannetn
                                                                                                                                          660
 ganattccac thncgcctnc chtchatchg naanachaaa nacthtctna cccnggggat
                                                                                                                                          720
 gggnncctcg ntcatcctct ctttttcnct accnccnntt ctttgcctct ccttngatca
780tccaaccntc gntggccntn cccccccnnn tcctttnccc
820
             <210> 27
              <211> 818
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(818)
              <223> n = A,T,C or G
              <400> 27
  tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct
                                                                                                                                            60
                                                                                                                                          120
  tqtttcttct ccqagcccca ggcagcggtg attcagccct gcccaacctg attctgatga
  ctqcqqatqc tqtqacqqac ccaaggggca aatagggtcc cagggtccag ggaggggcgc
                                                                                                                                          180
  ctgctgagca cttccgcccc tcaccctgcc cagcccctgc catgagctct gggctgggtc
                                                                                                                                          240
  teegeeteea gggttetget etteeangea ngeeancaag tggegetggg ceacactgge
                                                                                                                                          300
  ttetteetge ecenteeetg getetgante tetgtettee tgteetgtge angeneettg
                                                                                                                                          360
  gatctcagtt tecetenete anngaactet gtttetgann tetteantta actntgantt
                                                                                                                                          420
  tatnacenan tggnetgtne tgtennactt taatgggeen gaeeggetaa teeeteeete
                                                                                                                                          480
  netecettee anttennnna accngettne ententetee centaneceg eengggaane
                                                                                                                                          540
                                                                                                                                          600
  ctcctttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc
  ctqntnnccc cnctcncnnt tncctcgtcc cnncnncgcn nngcannttc ncngtcccnn
                                                                                                                                          660
  tnnctcttcn ngtntcgnaa ngntcncntn tnnnnngncn ngntnntncn tccctctcnc
                                                                                                                                          720
  connitgo to the tenter of the 
                                                                                                                                          780
  cccnnccccc ngnattaagg cctccnntct ccggccnc
                                                                                                                                          818
              <210> 28
              <211> 731
```

BNSDOCID: <WO___0004149A2_I_>

<212> DNA

```
<213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(731)
       <223> n = A, T, C or G
       <400> 28
aggaagggg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg
                                                                         60
tcccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt
                                                                        120
gattnaaccc cattgtatgg agnnaaaggn tttnagggat ttttcggctc ttatcagtat
                                                                        180
ntanattcct gtnaatcgga aaatnatntt tcnncnggaa aatnttgctc ccatccgnaa
                                                                        240
attnctcccg ggtagtgcat nttngggggn cngccangtt tcccaggctg ctanaatcgt
                                                                        300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatcen taccegactg
                                                                        360
tnnnttncct tcgccctntg actctgcnng agcccaatac ccnngngnat gtcncccngn
                                                                        420
nnngcgncnc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn
                                                                        480
cgtttcncat naaggcactt tngcctcatc caaccnctng ccctcnncca tttngccgtc
                                                                       540
nggttenect acgetnntng encetnnntn ganattttne cegeetnggg naanceteet
                                                                       600
gnaatgggta gggnettnte ttttnacenn gnggtntaet aatennetne acgentnett
                                                                       660
tetenacece ecceetttt caateceane ggenaatggg gteteceenn egangggggg
                                                                       720
nnncccannc c
                                                                       731
      <210> 29
      <211> 822
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(822)
      <223> n = A,T,C or G
      <400> 29
actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat
                                                                        60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt
                                                                       120
atnitniacne teatanneet ennnaceeae teeetettaa eeentaetgi geetaingen
                                                                       180
tnnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc
                                                                       240
tenecatnin geetananta ngineatace etatacetae necaatgeta nnnetaanen
                                                                       300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc
                                                                       360
tactctgact cccacngcct annnattagc anchtccccc nachatntct caaccaaatc
                                                                       420
ntcaacaacc tatctanctg ttcnccaacc nttncctccg atccccnnac aaccccctc
                                                                       480
ccaaataccc nccacctgac ncctaacccn caccatcccg gcaagccnan ggncatttan
                                                                       540
ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccctaana
                                                                       600
aatnctcctn naatttactn ncantnccat caancccacn tgaaacnnaa cccctgtttt
                                                                       660
tanatecett etttegaaaa eenaeeettt annneeeaae etttngggee eeceenetne
                                                                       720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg
                                                                       780
canatectat cecttanttn ggggneeett neeengggee ee
                                                                       822
      <210> 30
      <211> 787
      <212> DNA
      <213> Homo sapien
      <220>
     <221> misc_feature
```

```
<222> (1)...(787)
      <223> n = A, T, C or G
      <400> 30
cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg
                                                                        60
ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt
                                                                       120
gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna
                                                                       180
gctqqaaqcc ctqqaqqqcc tctctcgcca gcctcccct tctctccacg ctctccangg
                                                                       240
acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga
                                                                       300
cccatggggc ctgnaaggcc agggtctcct ttgacaccat ctctcccgtc ctgcctggca
                                                                       360
ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt
                                                                       420
tcccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt
                                                                       480
qtqaaattqt ttntcccctc ncnattccnc ncnacatacn aacccggaan cataaagtgt
                                                                       540
taaaqcctqq qqqtnqcctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc
                                                                       600
ccgctttccn ttcnggaaaa ctgtcntccc ctgcnttnnt gaatcggcca cccccngqq
                                                                       660
aaaageggtt tgenttttng ggggnteett cenetteece cetenetaan eeetnegeet
                                                                       720
cggtcgttnc nggtngcggg gaangggnat nnnctcccnc naagggggng agnnngntat
                                                                       780
                                                                       787
ccccaaa
      <210> 31
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(799)
      <223> n = A,T,C or G
      <400> 31
ttttttttt ttttttggc gatgctactg tttaattgca ggaggtgggg gtytgtgtac
                                                                        60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc
                                                                       120
aacaaaggac teetgeagee ttetetgtet gtetettgge geaggeacat ggggaggeet
                                                                       180
cccgcagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg
                                                                       240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca
                                                                       300
ggggaccttc tgttctccca nggnaacttc ntnnatctcn aaagaacaca actgtttctt
                                                                       360
engeanttet ggetgtteat ggaaageaca ggtgteenat tinggetggg actiggtaca
                                                                       420
tatggttccg gcccacctct cccntcnaan aagtaattca ccccccccn ccntctnttg
                                                                       480
cctgggccct taantaccca caccggaact canttantta ttcatcting gntgggcttg
                                                                       540
ntnatchech cetgaangeg ceaagttgaa aggeeaegee gtheeenete eecatagnan
                                                                       600
nttttnnent canetaatge eeceeengge aaenateeaa teeeeeceen tgggggeeee
                                                                       660
ageceangge eccegneteg ggnnneengn enegnantee ecaggntete ecantengne
                                                                       720
connngence ecegeacgea gaacanaagg ntngageene egeannnnnn nggtnnenae
                                                                       780
                                                                       799
ctcgccccc ccnncgnng
      <210> 32
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
      <223> n = A, T, C \text{ or } G
```

```
<400> 32
 60
 ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac
                                                                      120
 ggcaacaggc tccggcggcg gcggcggcgg ccctacctgc ggtaccaaat ntgcagcctc
                                                                      180
 cgctcccgct tgatnttcct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn
                                                                      240
 ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc
                                                                      300
nattaggaat agtggtntta cccnccnccg ttggcncact ccccntggaa accacttntc
                                                                      360
gcggctccgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt
                                                                      420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc
                                                                      480
ggnccatgtc ttnncggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac
                                                                      540
ccaaaagttc ttgnggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcatc
                                                                      600
ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt
                                                                      660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnnctctaa ngaaaacncc
                                                                      720
ntcctnnnca ccatccccc nngnnacgnc tancaangna tcccttttt tanaaacggg
                                                                      780
 cccccncq
                                                                      789
      <210> 33
       <211> 793
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(793)
      <223> n = A,T,C or G
      <400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg
                                                                      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg
                                                                     120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana
                                                                     180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg
                                                                     240
gcacagatge etgtgtgaet eeggttetga ettttgagga ggttgtteat eatgateaca
                                                                     300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac
                                                                     360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc
                                                                     420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct
                                                                     480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac
                                                                     540
acaacatacg anceggaage atnaaatttt aaageetggn ggtngeetaa tgantgaact
                                                                     600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt
                                                                     660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg
                                                                     720
cgcncttccc gctttctcgc ttcctgaant ccttccccc ggtctttcgg cttgcggcna
                                                                     780
acggtatcna cct
                                                                     793
      <210> 34
      <211> 756
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(756)
      <223> n = A,T,C or G
      <400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt
                                                                     60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg
                                                                    120
```

```
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtga catactggag
                                                                       180
atcggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatggcc
                                                                       240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac
                                                                       300
cagetettgg geeteaacet eetetteetg etgteecaga acegggtgge tgantnecae
                                                                       360
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca
                                                                       420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcctgg ccnagggtaa
                                                                       480
catcccccgc cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg
                                                                       540
aaaatcgcng ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg
                                                                       600
athonotagt notagaateg geoegecate geggtggane etceaacett tegttneeet
                                                                       660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acnccngttn cctgtgttga
                                                                       720
aattnttaac ccccacaat tccacgccna cattng
                                                                       756
      <210> 35
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 35
ggggatctct anatchacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg
                                                                        60
aacaggatct tgcccttgaa gctctcggct gctgtnttta agttgctcag tctgccgtca
                                                                       120
tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt cacctccaat
                                                                       180
aatcttengg getgtetget eggtgaacte gatgaenang ggeagetggt tgtgtntgat
                                                                       240
aaantccanc angtteteet tggtgacete eeetteaaag ttgtteegge etteateaaa
                                                                       300
cttctnnaan angannance canctttgte gagetggnat ttgganaaca egteacegtt
                                                                       360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt
                                                                       420
ggcncaaatc cgactccccn tccttgaaag aagccnatca caccccctc cctggactcc
                                                                       480
nncaangact ctnccgctnc cccntccnng cagggttggt ggcannccgg gcccntgcgc
                                                                       540
ttcttcagcc agttcacnat nttcatcagc ccctctgcca gctgttntat tccttggggg
                                                                       600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcnccnt
                                                                       660
acninctggg ccgggttcaa anteceteen ttgnennten cetegggeca ttetggattt
                                                                       720
nccnaacttt ttccttcccc cnccccncgg ngtttggntt tttcatnggg ccccaactct
                                                                       780
getnttggcc anteceetgg gggentntan enceeetnt ggtecentng ggcc
                                                                       834
      <210> 36
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(814)
      <223> n = A,T,C or G
      <400> 36
cggncgcttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn
                                                                        60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca
                                                                       120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggtctctcc accccctgta
                                                                       180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact
                                                                       240
                                                                       300
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca
                                                                       360
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca
```

WO 00/04149

```
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc
                                                                        420
 antganctgg aaggeetgaa nettagtete caaaagtete ngeecacaag aceggeeace
                                                                        480
 aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag
                                                                        540
 gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc
                                                                        600
 cttccggtct gatccnaaag gaatgttcct gggtcccant ccctcctttg ttncttacgt
                                                                        660
 tgtnttggac centgetngn atnacecaan tganatecec ngaageacec tneeetgge
                                                                        720
 atttganttt entaaattet etgeeetaen netgaaagea enatteeetn ggeneenaan
                                                                        780
 ggngaactca agaaggtctn ngaaaaacca cncn
                                                                        814
       <210> 37
       <211> 760
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(760)
       <223> n = A, T, C \text{ or } G
       <400> 37
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg
                                                                         60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt gcagagtcct
                                                                        120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg
                                                                        180
tcnaanccac tcgtgtattt ttcacangca gcctcctccg aagcntccgg gcagttgggg
                                                                        240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt
                                                                        300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat
                                                                        360
cncctnance caaactgeet etcaaaggee acettgeaca eccegacagg etagaaatge
                                                                        420
actettette ecaaaggtag ttgttettgt tgeecaagea neeteeanea aaceaaaane
                                                                       480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccggcngn
                                                                       540
gancencett gtttgaatge naaggnaata atecteetgt ettgettggg tggaanagea
                                                                       600
caattgaact gttaacnttg ggccgngttc cnctngggtg gtctgaaact aatcaccgtc
                                                                       660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtnnttt
                                                                       720
ctcctctncc ctaaaaatcg tnttccccc ccntanggcg
                                                                       760
      <210> 38
      <211> 724
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(724)
      <223> n = A,T,C or G
      <400> 38
ttttttttt ttttttttt tttttttt tttttaaaaa ccccctccat tgaatgaaaa
                                                                        60
cttccnaaat tgtccaaccc cctcnnccaa atnnccattt ccgggggggg gttccaaacc
                                                                       120
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa
                                                                       180
aatttaaccc attatnaact taaatneetn gaaaceentg gntteeaaaa atttttaace
                                                                       240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaaggtt
                                                                       300
ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt
                                                                       360
tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt
                                                                       420
tttttgaatt ggaaattccn ngggaattna ccggggtttt tcccntttgg gggccatncc
                                                                       480
cccnctttcg gggtttgggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana
                                                                       540
aaaaaactcc caagnnttaa ttngaatntc ccccttccca ggccttttgg gaaaggnggg
                                                                       600
```

```
tttntggggg congggantt cnttcccccn ttnccncccc cccccnggt aaanggttat
                                                                       660
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccgggncg
                                                                       720
                                                                       724
gccg
      <210> 39
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(751)
      <223> n = A,T,C or G
      <400> 39
tttttttttt tttttctttg ctcacattta atttttattt tgatttttt taatgctgca
                                                                        60
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt
                                                                       120
tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc tttttctgta
                                                                       180
ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt
                                                                       240
cgcaaaatca ctcgggggaa nggaaaggtt gctttgttaa tcatgcccta tggtgggtga
                                                                       300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc tttaattana
                                                                       360
cttqqqqqtt ccctcccan accaacccn ctgacaaaaa gtgccngccc tcaaatnatg
                                                                       420
tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa
                                                                       480
tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn
                                                                       540
                                                                       600
ccctcaanch aattnctnng ccccggtcnc gentnngtcc cncccgggct ccgggaanth
caccccnga annonntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc
                                                                       660
cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgnnc cnnaaaatgn
                                                                       720
                                                                       751
nnnncncctc cnctngtccn naatcnccan c
      <210> 40
      <211> 753
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(753)
      <223> n = A,T,C or G
      <400> 40
                                                                        60
gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat
                                                                       120
agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg
cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa
                                                                       180
                                                                       240
tqqtctqqaa gcqqcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact
                                                                       300
teteaaaqtt eeaqqeaaen tegttgegae acaceggaga eeaggtgatn agettggggt
                                                                       360
eggteataan egeggtggeg tegtegetgg gagetggeag ggeeteeege aggaaggena
                                                                       420
ataaaaggtg cgccccgca ccgttcanct cgcacttctc naanaccatg angttgggct
cnaacccacc accannecgg actteettga nggaatteec aaatetette gntettggge
                                                                       480
ttctnctgat gccctanctg gttgcccngn atgccaanca nccccaance ccggggtcct
                                                                       540
aaancacccn cctcctcntt tcatctgggt tnttntcccc ggaccntggt tcctctcaag
                                                                       600
ggancccata totonaccan tactoacont noceccoont gnnacccano ottotanngn
                                                                       660
ttcccncccg ncctctggcc cntcaaanan gcttncacna cctgggtctg ccttccccc
                                                                       720
tnccctatct gnaccccncn tttgtctcan tnt
                                                                       753
```

<210> 41

```
<211> 341
       <212> DNA
       <213> Homo sapien
       <400> 41
 actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaatg
                                                                         60
 agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac
                                                                        120
 ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt
                                                                        180
 tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag
                                                                        240
 tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat
                                                                        300
 ttttactttt tgattaattg tgttttatat attagggtag t
                                                                        341
       <210> 42
       <211> 101
       <212> DNA
       <213> Homo sapien
       <400> 42
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat
                                                                         60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a
                                                                        101
      <210> 43
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 43
acatettigt tacagietaa gaigigitet taaateacea tieetteetg gieeteacee
                                                                         60
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat
                                                                        120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca
                                                                        180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat
                                                                        240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cgggggccgc
                                                                       300
tcqaa
                                                                       305
      <210> 44
      <211> 852
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(852)
      <223> n = A,T,C or G
      <400> 44
acataaatat cagagaaaag tagtetttga aatatttacg tecaggagtt etttgttet
                                                                        60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt
                                                                       120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct
                                                                       180
ccagaatttc tcttttgtag taatatctca tagctcggct gagcttttca taggtcatgc
                                                                       240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga
                                                                       300
agacgccctc agatcggtct tcccatttta ttaatcctgg gttcttgtct gggttcaaga
                                                                       360
ggatgtcgcg gatgaattcc cataagtgag tccctctcgg gttgtgcttt ttggtgtggc
                                                                       420
acttggcagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca ggaaggtgac
                                                                       480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg
                                                                       540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatggaag
                                                                       600
```

```
geteagtittg ticagtettg acaatgacat tgtgtgtgga etggaacagg teactactge
                                                                       660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg
                                                                       720
ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact
                                                                       780
cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact
                                                                       840
cccacacctg gt
                                                                       852
      <210> 45
      <211> 234
      <212> DNA
      <213> Homo sapien
      <400> 45
acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg
                                                                        60
agtotgacac catcoggago atcagoattg ottogoagtg cootacogog gggaactott
                                                                       120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg
                                                                       180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacccg ctgt
                                                                       234
      <210> 46
      <211> 590
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(590)
      <223> n = A,T,C or G
      <400> 46
actitttatt taaatgitta taaggcagat ctatgagaat gatagaaaac atggigtgia
                                                                        60
atttgatagc aatattttgg agattacaga gttttagtaa ttaccaatta cacagttaaa
                                                                       120
aagaagataa tatatteeaa geanataeaa aatatetaat gaaagateaa ggeaggaaaa
                                                                       180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta
                                                                       240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat
                                                                       300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat
                                                                       360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc
                                                                       420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag
                                                                       480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct
                                                                       540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt
                                                                       590
      <210> 47
      <211> 774
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(774)
      <223> n = A,T,C or G
      <400> 47
acaagggggc ataatgaagg agtggggana gattttaaag aaggaaaaaa aacgaggccc
                                                                        60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac
                                                                       120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg
                                                                       180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa
                                                                       240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct
                                                                       300
```

WO 00/04149

```
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctcctgtgtg
                                                                         360
 ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc
                                                                         420
 ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt
                                                                         480
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc
                                                                         540
 acggcatggg aagcctttct gacttgcctg attactccag catcttggaa caatccctga
                                                                         600
 ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttggagcc
                                                                         660
 aggetgetgg etteaaattn tggeteattt acgagetatg ggaeettggg caagtnatet
                                                                         720
 tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt
                                                                         774
       <210> 48
       <211> 124
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(124)
       <223> n = A,T,C or G
       <400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt
                                                                         60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact
                                                                        120
tggt
                                                                        124
      <210> 49
      <211> 147
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(147)
      \langle 223 \rangle n = A,T,C or G
      <400> 49
gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt
                                                                         60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt
                                                                        120
ttagggcacc catatcccaa gcantgt
                                                                        147
      <210> 50
      <211> 107
      <212> DNA
      <213> Homo sapien
      <400> 50
acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatattgc
                                                                        60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt
                                                                        107
      <210> 51
      <211> 204
      <212> DNA
      <213> Homo sapien
gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg
                                                                        60
```

```
cqqqaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag
                                                                       120
qccttqcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttggcca
                                                                       180
cctccctttt gggaccagca atgt
                                                                       204
      <210> 52
      <211> 491
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(491)
      <223> n = A,T,C or G
      <400> 52
acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta
                                                                        60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca
                                                                       120
ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa
                                                                       180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt
                                                                       240
tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtncc ctcagtccca
                                                                       300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc
                                                                       360
atgcaacagt gtcttttctt tnctttttct ttttttttt ttacaggcac agaaactcat
                                                                       420
caattttatt tggataacaa agggtctcca aattatattg aaaaataaat ccaagttaat
                                                                       480
atcactcttg t
                                                                       491
      <210> 53
      <211> 484
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(484)
      <223> n = A,T,C or G
      <400> 53
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga
                                                                        60
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac
                                                                       120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct
                                                                       180
caatcaaatc tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct
                                                                       240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc
                                                                       300
agetttgant ttetttgtge tgatangagg aaaggetgaa ttacettgtt geeteteeet
                                                                       360
aatgattggc aggtenggta aatnecaaaa catattecaa etcaacaett etttteeneg
                                                                       420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc
                                                                       480
cant
                                                                       484
      <210> 54
      <211> 151
      <212> DNA
      <213> Homo sapien
      <400> 54
actaaacctc gtgcttgtga actccataca gaaaacggtg ccatccctga acacggctgg
                                                                        60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag
                                                                       120
tctatgtcct ctcaagtgcc tttttgtttg t
                                                                       151
```

WO 00/04149 PCT/US99/15838

```
<210> 55
       <211> 91
       <212> DNA
       <213> Homo sapien
       <400> 55
 acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc
                                                                          60
 gccctccagt ggatactcga gccaaagtgg t
                                                                          91
       <210> 56
       <211> 133
       <212> DNA
       <213> Homo sapien
       <400> 56
ggcggatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact
                                                                          60
tggatttttg gtatctgtgg gttgggggga cggtccagga accaataccc catggatacc
                                                                         120
 aagggacaac tgt
                                                                         133
       <210> 57
       <211> 147
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(147)
      <223> n = A,T,C or G
      <400> 57
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc
                                                                         60
gactgggage tgagecette cetttgegee tgeeteagag gattgttgee gacntgcana
                                                                        120
tctcantggg ctggatncat gcagggt
                                                                        147
      <210> 58
      <211> 198
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(198)
      <223> n = A,T,C \text{ or } G
      <400> 58
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc
                                                                         60
tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta
                                                                        120
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt
                                                                        180
ttgacttcta agtttggt
                                                                        198
      <210> 59
      <211> 330
      <212> DNA
      <213> Homo sapien
```

<400> 59				
acaacaaatg ggttgtgagg aagtcttatc ccattgaaaa ttatcattaa tgattttaaa cacctgtgct agcttgctaa aatgggagtt tacagtcaat aaatgacaaa gccagggcct cagaaggaat ctattttatc acatggatct tttcgtcttt attggacttc tttgaagagt	tgacaagtta aactctagag acaggtggtt	tcaaaaactc caaatatagt tccagacttt	actcaatttt atcttctgaa ccagacccag	60 120 180 240 300 330
<210> 60 <211> 175 <212> DNA <213> Homo sapien		,		
<400> 60 accgtgggtg ccttctacat tcctgacggc gtcgtgggct ccttcctctt catcctcatc tcctggaacc agcggtggct gggcaaggcc	cagctggtgc	tgctcatcga	ctttgcgcac	60 120 175
<210> 61 <211> 154 <212> DNA <213> Homo sapien				
<400> 61 accccacttt tcctcctgtg agcagtctgg ggttgttgct cttcaacagt atcctccct tggactgcac agccccgggg ctccacattg	ttccggatct			60 120 154
<210> 62 <211> 30 <212> DNA <213> Homo sapien				
<400> 62 cgctcgagcc ctatagtgag tcgtattaga				30
<210> 63 <211> 89 <212> DNA <213> Homo sapien				
<400> 63 acaagtcatt tcagcaccct ttgctcttca ctgtatgaat aaaaatggtt atgtcaagt	aaactgacca	tcttttatat	ttaatgcttc	60 89
<210> 64 <211> 97 <212> DNA <213> Homo sapien				
<400> 64 accggagtaa ctgagtcggg acgctgaatc		aataaataaa	ggttctgcag	60
aatcagtgca tccaggattg gtccttggat	ciggggt			97

```
<210> 65
       <211> 377
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(377)
       \langle 223 \rangle n = A,T,C or G
       <400> 65
 acaacaanaa ntcccttctt taggccactg atggaaacct ggaaccccct tttgatggca
                                                                          60
 gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc
                                                                         120
 ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggt
                                                                         180
 tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa
                                                                         240
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg
                                                                         300
 tgggggtgaa ctacccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag
                                                                         360
 gggcgggagg agcatgt
                                                                         377
       <210> 66
       <211> 305
       <212> DNA
       <213> Homo sapien
       <400> 66
acgcctttcc ctcagaattc agggaagaga ctgtcgcctg ccttcctccg ttgttgcgtg
                                                                         60
agaacccgtg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg
                                                                        120
aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct
                                                                        180
tectecacte taagggatat caacactgee cageacaggg geeetgaatt tatgtggttt
                                                                        240
ttatatattt tttaataaga tgcactttat gtcattttt aataaagtct gaagaattac
                                                                        300
tgttt
                                                                        305
      <210> 67
      <211> 385
      <212> DNA
      <213> Homo sapien
      <400> 67
actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga
                                                                         60
ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc
                                                                        120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc
                                                                        180
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg
                                                                        240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg
                                                                        300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac
                                                                        360
catagtttct gtgctagtgg accgt
                                                                        385
      <210> 68
      <211> 73
      <212> DNA
      <213> Homo sapien
      <400> 68
acttaaccag atatatttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa
                                                                         60
gtttttttaa tgg
                                                                         73
```

```
<210> 69
      <211> 536
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(536)
      \langle 223 \rangle n = A,T,C or G
      <400> 69
actagtecag tgtggtggaa ttecattgtg ttgggggete teacceteet etectgeage
                                                                         60
tecagetttg tgetetgeet etgaggagae catggeecag catetgagta ecetgetget
                                                                        120
cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat
                                                                        180
cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt
                                                                        240
cgccatcage gagtataaca aggecaccaa agatgactae tacagaegte egetgegggt
                                                                        300
actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg
                                                                        360
ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc
                                                                        420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca
                                                                        480
gaangteeet gggtgaaate caggtgteaa gaaateetan ggatetgttg ceagge
                                                                        536
      <210> 70
      <211> 477
      <212> DNA
      <213> Homo sapien
     <400> 70
atqaccecta acaggggeee tetcageeet cetaatgace teeggeetag ecatgtgatt
                                                                         60
tcacttccac tccataacgc tcctcatact aggcctacta accaacacac taaccatata
                                                                        120
ccaatqatqq cgcgatgtaa cacgagaaag cacataccaa ggccaccaca caccacctgt
                                                                        180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc
                                                                        240
agggattttt ctgagccttt taccactcca gcctagcccc tacccccaa ctaggagggc
                                                                        300
actqqcccc aacaqqcatc accccqctaa atcccctaga agtcccactc ctaaacacat
                                                                        360
ccgtattact cgcatcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca
                                                                        420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt
                                                                        477
      <210> 71
      <211> 533
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(533)
      <223> n = A, T, C \text{ or } G
      <400> 71
agagetatag gtacagtgtg ateteagett tgcaaacaca ttttetacat agatagtact
                                                                         60
aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattggttta
                                                                        120
tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat
                                                                        180
attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt
                                                                        240
taaataaagg tttgtcatct ttaaaaatac agcaatatgt gactttttaa aaaagctgtc
                                                                        300
aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca
                                                                        360
agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg
                                                                        420
cttcgtaatt ttggagtang aggttccctc ctcaattttg tatttttaaa aagtacatgg
                                                                        480
taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc
                                                                        533
```

WO 00/04149 PCT/US99/15838

```
<210> 72
       <211> 511
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(511)
       <223> n = A,T,C or G
       <400> 72
tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta
                                                                       60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa
                                                                      120
aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga
                                                                      180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt
                                                                      240
gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca
                                                                      300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac
                                                                      360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctgttatg
                                                                      420
atttctctcc attgcagcna naaacccgtt cttctaagca aacncaggtg atgatggcna
                                                                      480
aaatacaccc cctcttgaag naccnggagg a
                                                                      511
      <210> 73
      <211> 499
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(499)
      <223> n = A,T,C or G
      <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac
                                                                      60
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc
                                                                     120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta
                                                                     180
caagtgagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc agggtgcatc
                                                                     240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca
                                                                     300
360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc
                                                                     420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact
                                                                     480
gtcctttcct aantaaaat
                                                                     499
      <210> 74
      <211> 537
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(537)
      <223> n = A, T, C \text{ or } G
      <400> 74
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat
                                                                      60
```

```
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact
                                                                       120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa
                                                                       180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga
                                                                       240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaaatgg taatcattag
                                                                       300
qqcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc
                                                                       360
cagtttgctt gatatatttg ttgatattaa gattcttgac ttatattttg aatgggttct
                                                                       420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat
                                                                       480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt
                                                                       537
      <210> 75
      <211> 467
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(467)
      <223> n = A, T, C \text{ or } G
      <400> 75
caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc
                                                                        60
tgcatattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca
                                                                       120
cctqctqtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg
                                                                       180
tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga
                                                                       240
totagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta
                                                                       300
tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa
                                                                       360
caatqaqqaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc
                                                                       420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn
                                                                       467
      <210> 76
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(400)
      <223> n = A,T,C or G
      <400> 76
aagetgacag cattegggee gagatgtete geteegtgge ettagetgtg etegegetae
                                                                        60
tetetette tggeetggag getateeage gtaeteeaaa gatteaggtt taeteaegte
                                                                       120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat
                                                                       180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag
                                                                       240
acttgtettt cageaaggae tggtetttet atetettgta etacaetgaa tteaeceeca
                                                                       300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng
                                                                       360
ttnagtggga tcganacatg taagcagcan catgggaggt
                                                                       400
      <210> 77
      <211> 248
      <212> DNA
      <213> Homo sapien
      <400> 77
ctggagtgcc ttggtgtttc.aagcccctgc aggaagcaga atgcaccttc tgaggcacct
                                                                        60
```

```
ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc
                                                                          120
 caggcactgt tcatctcagc ttttctgtcc ctttgctccc ggcaagcgct tctgctgaaa
                                                                          180
 gttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa
                                                                         240
 aaaaaaa
                                                                         248
       <210> 78
       <211> 201
       <212> DNA
       <213> Homo sapien
       <400> 78
 actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
                                                                          60
 tcacccagac cccgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac
                                                                         120
 tctgctactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct
                                                                         180
 gatttaaaaa aaaaaaaaa a
                                                                         201
       <210> 79
       <211> 552
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(552)
       \langle 223 \rangle n = A, T, C or G
       <400> 79
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg
                                                                          60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt
                                                                         120
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag
                                                                         180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt
                                                                         240
atgcaagtta gtaattactc agggttaact aaattacttt aatatgctgt tgaacctact
                                                                         300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga
                                                                         360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta
                                                                        420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac
                                                                        480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa
                                                                        540
aaaaaaaaa aa
                                                                        552
      <210> 80
      <211> 476
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(476)
      <223> n = A, T, C \text{ or } G
      <400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga
                                                                         60
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct
                                                                        120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt
                                                                        180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta
                                                                        240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac
                                                                        300
tettetaagt eetetteeag eeteactitg agteeteett gggggttgat aggaaninte
                                                                        360
```

```
tottqqcttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaaat
                                                                        420
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa
                                                                        476
      <210> 81
      <211> 232
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(232)
      <223> n = A, T, C \text{ or } G
      <400> 81
tttttttttg tatgccntcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt
                                                                         60
ttettetgta tetttettt etgggggate tteetggete tgeeceteea tteecageet
                                                                        120
ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcctggtag cccctcagag
                                                                        180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct
                                                                        232
      <210> 82
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(383)
      <223> n = A,T,C or G
      <400> 82
aggegggage agaagetaaa gecaaageee aagaagagtg geagtgeeag caetggtgee
                                                                         60
agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtggc ttcagtgctg
                                                                        120
                                                                        180
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt
                                                                        240
gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac
                                                                        300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg
                                                                        360
ccatttcaaa aaaaaaaaaa aaa
                                                                        383
      <210> 83
      <211> 494
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(494)
      <223> n = A,T,C or G
      <400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca
                                                                         60
gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc
                                                                        120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa
                                                                        180
acgettcaag gtgetcatga cecageaace gegeeetgte etetgagggt cettaaactg
                                                                        240
                                                                        300
atgtcttttc tgccacctgt tacccctcgg agactccgta accaaactct tcggactgtg
agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat
                                                                        360
```

```
tatgcttgtg tgaggcaatc atggtggcat cacccatnaa gggaacacat ttgantttt
                                                                        420
 tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta
                                                                        480
 aaaaaaaaa aaaa
                                                                        494
       <210> 84
       <211> 380
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(380)
       <223> n = A,T,C or G
       <400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca
                                                                         60
agtatectge geogegicti etacegicee tacetgeaga tettegggea gatteceeag
                                                                        120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg
                                                                        180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctggtg
                                                                        240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg
                                                                        300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc
                                                                        360
agcgttnccg cctcatccgg
                                                                        380
      <210> 85
      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(481)
      <223> n = A,T,C or G
      <400> 85
gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                        60
tnccategic atacigtagg titgecacea ecteetgeat etiggggegg etaatateea
                                                                       120
ggaaactete aatcaagtea eegtenatna aacetgtgge tggttetgte tteegetegg
                                                                       180
tgtgaaagga tetecagaag gagtgetega tettececae aettttgatg aetttattga
                                                                       240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc
                                                                       300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac
                                                                       360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa
                                                                       420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnngc gcntnccttt
                                                                       480
                                                                       481
      <210> 86
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(472)
      <223> n = A,T,C or G
      <400> 86
```

```
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt
                                                                        60
acttqqaaaa gcaacttnaa gcctggacac tggtattaaa attcacaata tgcaacactt
                                                                       120
taaacaqtqt qtcaatctgc tcccttactt tgtcatcacc agtctgggaa taaggqtatq
                                                                       180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga
                                                                       240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt
                                                                       300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg
                                                                       360
atatntgage ggaagantag cetttetaet teaceagaea caacteettt catattggga
                                                                       420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg
                                                                       472
      <210> 87
      <211> 413
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(413)
      <223> n = A, T, C \text{ or } G
      <400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                        60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                       120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                       180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                       240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg
                                                                       300
ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa
                                                                       360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt
                                                                       413
      <210> 88
      <211> 448
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(448)
      <223> n = A,T,C or G
      <400> 88
cgcagcgggt cotototate tagetccage ctotogcotg coccactocc cgcgtcccgc
                                                                        60
gtectageen accatggeeg ggeeeetgeg egeeeegetg eteetgetgg ecateetgge
                                                                       120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc ggcaagccgc cgcgcctggt
                                                                       180
gggaggccca tggaccccgc gtggaagaag aaggtgtgcg gcgtgcactg gactttgccg
                                                                       240
teggenanta caacaaacce geaacnactt ttacenagen egegetgeag gttgtgeege
                                                                       300
cccaancaaa ttgttactng qqqtaantaa ttcttggaag ttgaacctgg gccaaacnng
                                                                       360
tttaccaqaa ccnaqccaat tnqaacaatt ncccctccat aacaqcccct tttaaaaaaqq
                                                                       420
gaancantcc tgntcttttc caaatttt
                                                                       448
      <210> 89
      <211> 463
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
```

```
<222> (1)...(463)
       <223> n = A,T,C or G
       <400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca
                                                                         60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc
                                                                        120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt
                                                                        180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc
                                                                        240
tttnatgttn agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg
                                                                        300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn
                                                                        360
aattetete ecatannaaa acceangece ttggganaat ttgaaaaang gnteettenn
                                                                        420
aattcnnana anttcagntn tcatacaaca naacngganc ccc
                                                                        463
       <210> 90
       <211> 400
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(400)
       <223> n = A,T,C or G
       <400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt
                                                                         60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat
                                                                        120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact
                                                                        180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct
                                                                       240
cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtccct
                                                                       300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa
                                                                       360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca
                                                                       400
      <210> 91
      <211> 480
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(480)
      <223> n = A, T, C or G
      <400> 91
gageteggat ecaataatet ttgtetgagg geageacaea tatneagtge eatggnaact
                                                                        60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                       120
atgcctcttt gactaccgtg tgccagtgct ggtgattctc acacacctcc nnccgctctt
                                                                       180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga
                                                                       240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt
                                                                       300
tgtcaatact aaccegetgg tttgcctcca tcacatttgt gatctgtagc tctggataca
                                                                       360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt
                                                                       420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa
                                                                       480
      <210> 92
      <211> 477
      <212> DNA
```

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(477)
      <223> n = A, T, C \text{ or } G
      <400> 92
atacagecca nateceaeca egaagatgeg ettgttgaet gagaaectga tgeggteaet
                                                                          60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt
                                                                         120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt
                                                                         180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc
                                                                         240
tgcagcgaaa ctcctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca
                                                                         300
gaacetteeg cetgttetet ggegteacet geagetgetg cegetnacae teggeetegg
                                                                         360
accageggae aaacggegtt gaacageege accteaegga tgeecantgt gtegegetee
                                                                         420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg
                                                                         477
      <210> 93
      <211> 377
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(377)
      \langle 223 \rangle n = A,T,C or G
      <400> 93
gaacggctgg accttgcctc gcattgtgct gctggcagga ataccttggc aagcagctcc
                                                                         60
agtecgagea gecceagace getgeegeee gaagetaage etgeetetgg cetteceete
                                                                         120
cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn
                                                                        180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaat ttccaaacaa
                                                                        240
caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta
                                                                        300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa
                                                                        360
ataaatatat tattaaa
                                                                        377
      <210> 94
      <211> 495
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(495)
      \langle 223 \rangle n = A,T,C or G
      <400> 94
ccctttgagg ggttagggtc cagttcccag tggaagaaac aggccaggag aantgcgtgc
                                                                         60
egagetgang cagattteec acagtgacee cagageeetg ggetatagte tetgaceeet
                                                                        120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg
                                                                        180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgccccc
                                                                        240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaa
                                                                        300
tgcaagctca ccaaggtccc ctctcagtcc cttccctaca ccctgaacgg ncactggccc
                                                                        360
acacceacce agancaneea eeegecatgg ggaatgtnet caaggaateg engggeaacg
                                                                        420
tggactetng tecennaagg gggeagaate tecaatagan gganngaace ettgetnana
                                                                        480
```

```
aaaaaaana aaaaa
                                                                         495
       <210> 95
       <211> 472
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(472)
       <223> n = A,T,C or G
       <400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                          60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt
                                                                         120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact
                                                                         180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt
                                                                         240
atgatgaaaa gcaatagata tatattettt tattatgttn aattatgatt gecattatta
                                                                         300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac
                                                                         360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata
                                                                         420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at
                                                                         472
       <210> 96
       <211> 476
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(476)
      <223> n = A,T,C \text{ or } G
      <400> 96
ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat
                                                                         60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt
                                                                        120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt
                                                                        180
attetteaca gtagatgatg aaagagteet ceagtgtett gngeanaatg ttetagntat
                                                                        240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat
                                                                        300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct
                                                                        360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt
                                                                        420
tacaaagtct atcttcctca nangtctgtn aaggaacaat ttaatcttct agcttt
                                                                        476
      <210> 97
      <211> 479
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(479)
      <223> n = A,T,C or G
      <400> 97
actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata
                                                                        60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatgaa acacagctta
                                                                       120
```

caatcgcaaa tcaaaactca gattgtgctc cttcggatat caggctacta gaattctgtt gtgattatna aattaatcac ntnnttttta natcaaagta ttcnatctta tttttcccn	gattgtttct attggatatn aaatttcact ttttgtgttt	canatcttgg tgagagcatg tatacctgct ggaantgtnn	gcaatnttcc aaatttttaa atcagcagct aaatgaaatc	ttagtcaaat naatacactt agaaaaacat tgaatgtggg	180 240 300 360 420 479
<210> 98 <211> 461 <212> DNA <213> Homo sapie	n				
<pre><400> 98 agtgacttgt cctccaacaa tgctagttcc tgtcatctat tcaactccag ctggattatt agtgattcag tttcctctac tgaagccact ctgaacacgc ttacctggag aaaagaggct ttaagaaaaa ctaccacatg tttggaataa tcttgacgct</pre>	tcgctactaa ttggagcctg ggatgagaga tggttatcta ttggctgggg ttgtgtatcc	atgcagactg caaatctatt ctggctcaag gatgagaaca accatcccat tggtgccggc	gaggggacca cctacttgta aatatcctca gagaaataaa tgaaccttct cgtttatgaa	aaaaggggca cggactttga tgcagcttta gtcagaaaat cttaaggact	60 120 180 240 300 360 420 461
<210> 99 <211> 171 <212> DNA <213> Homo sapie	en				
<pre><400> 99 gtggccgcgc gcaggtgttt cggcgcctct gcgggcccga cggtgagaaa agccttctct <210> 100</pre>	ggaggagcgg	ctggcgggtg	gggggagtgt	gacccaccct	60 120 171
<211> 269 <212> DNA <213> Homo sapie	n				
<pre><400> 100 cggccgcaag tgcaactcca cgactgcgac gacggcggcg aaggctgagc tgacgccgca cagccggaac agagcccggt cgagagatac gcaggtgcag</pre>	gcgacagtcg gaggtcgtgt gaagcgggag	caggtgcagc cacgtcccac	gcgggcgcct gaccttgacg	ggggtettge cegtegggga	60 120 180 240 269
<210> 101 <211> 405 <212> DNA <213> Homo sapie	en				
<pre><400> 101 ttttttttt ttttggaatc gctagcaagg taacagggta ttgattggtt tgtctttatg agtgggtgca ccctccctgt tgaccgtcat tttcttgaca</pre>	gggcatggtt ggggcggggt agaacctggt	acatgttcag ggggtagggg tacaaagctt	gtcaacttcc aaacgaagca ggggcagttc	tttgtcgtgg aataacatgg acctggtctg	60 120 180 240 300

```
ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttq
                                                                    360
 gatgatcagt acgaataccg aggcatattc tcatatcggt ggcca
                                                                    405
       <210> 102
      <211> 470
      <212> DNA
      <213> Homo sapien
      <400> 102
60
ggcacttaat ccatttttat ttcaaaatgt ctacaaattt aatcccatta tacggtattt
                                                                   120
tcaaaatcta aattattcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa
                                                                   180
atatacttct ttcagcaaac ttgttacata aattaaaaaa atatatacgg ctggtgtttt
                                                                   240
caaagtacaa ttatcttaac actgcaaaca ttttaaggaa ctaaaataaa aaaaaacact
                                                                   300
ccgcaaaggt taaagggaac aacaaattct tttacaacac cattataaaa atcatatctc
                                                                   360
aaatcttagg ggaatatata cttcacacgg gatcttaact tttactcact ttgtttattt
                                                                   420
ttttaaacca ttgtttgggc ccaacacaat ggaatccccc ctggactagt
                                                                   470
      <210> 103
      <211> 581
      <212> DNA
      <213> Homo sapien
      <400> 103
ttttttttt tttttttga cccccctctt ataaaaaaca agttaccatt ttatttact
                                                                    60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                   120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                   180
gaaaatette tetagetett ttgactgtaa atttttgact ettgtaaaac atecaaatte
                                                                   240
atttttcttg tctttaaaat tatctaatct ttccattttt tccctattcc aagtcaattt
                                                                   300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa
                                                                   360
agggaaaaca ggaagagaaa tggcacacaa aacaaacatt ttatattcat atttctacct
                                                                   420
acgttaataa aatagcattt tgtgaagcca gctcaaaaga aggcttagat ccttttatgt
                                                                   480
ccattttagt cactaaacga tatcaaagtg ccagaatgca aaaggtttgt gaacatttat
                                                                   540
tcaaaagcta atataagata tttcacatac tcatctttct g
                                                                   581
      <210> 104
      <211> 578
      <212> DNA
      <213> Homo sapien
      <400> 104
60
cactetetag atagggeatg aagaaaacte atettteeag etttaaaaata acaateaaat
                                                                  120
ctcttatgct atatcatatt ttaagttaaa ctaatgagtc actggcttat cttctcctga
                                                                  180
aggaaatctg ttcattcttc tcattcatat agttatatca agtactacct tgcatattga
                                                                  240
gaggtttttc ttctctattt acacatatat ttccatgtga atttgtatca aacctttatt
                                                                  300
ttcatgcaaa ctagaaaata atgtttcttt tgcataagag aagagaacaa tatagcatta
                                                                  360
caaaactgct caaattgttt gttaagttat ccattataat tagttggcag gagctaatac
                                                                  420
aaatcacatt tacgacagca ataataaaac tgaagtacca gttaaatatc caaaataatt
                                                                  480
aaaggaacat ttttagcctg ggtataatta gctaattcac tttacaagca tttattagaa
                                                                  540
tgaattcaca tgttattatt cctagcccaa cacaatgg
                                                                  578
     <210> 105
     <211> 538
```

<212> DNA

<213> Homo sapien

<400> 105			***		C 0
tttttttt tttttcagta					60
gaaaagtgcc ttacatttaa					120
gtcttgaaca ccaatattaa					180
aagatcatag agcttgtaag					240
aaatccacta ttagcaaata					300
ggggtgtcac tggtaaacca					360
tgtactttgc taatacgtgg					420
ggcgagaaat gaggaagaaa					480
agatatgttt cctttgccaa	tattaaaaaa	ataataatgt	ttactactag	tgaaaccc	538
<210> 106					
<211> 473					
<212> DNA					
<213> Homo sapie	n				
-400- 106					
<400> 106 ttttttttt tttttagtc	aagtttctat	ttttattata	attaaagtct	ragicatite	60
atttattagc tctgcaactt					120
					180
tttataaatg taaggtgcca					240
tctcccacca actaatgaac					300
gcaaacgcta attctcttct					
aatgcatcac aatctacaat					360
agactgtgtc tgtctgaatc					420
ccgcttcctc aaaggcgctg	ccacatttgt.	ggctctttgc	acttgtttca	aaa	473
<210> 107					
<210> 107 <211> 1621					
<211> 1621	en				
<211> 1621 <212> DNA <213> Homo sapie	n				
<211> 1621 <212> DNA <213> Homo sapie <400> 107		ggagetgtee	ggeet ggees	caaacccatt	60
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca	tctcggtcat				60 120
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg	tctcggtcat acttcggggc	gcgtgtggta	cgcgtggacc	ggcccggctc	120
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct	teteggteat acttegggge tgggeegggg	gcgtgtggta caagcgctcg	cgcgtggacc ctagtgctgg	ggcccggctc acctgaagca	120 180
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc	teteggteat acttegggge tgggeegggg tgeggegtet	gcgtgtggta caagcgctcg gtgcaagcgg	cgcgtggacc ctagtgctgg tcggatgtgc	ggcccggctc acctgaagca tgctggagcc	120 180 240
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg	teteggteat acttegggge tgggeegggg tgeggegtet agaaacteca	gcgtgtggta caagcgctcg gtgcaagcgg gctgggccca	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc	ggcccggctc acctgaagca tgctggagcc agcgggaaaa	120 180 240 300
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca	teteggteat acttegggge tgggeeggg tgeggegtet agaaaeteea ggetgagtgg	gcgtgtggta caagcgctcg gtgcaagcgg gctgggccca atttggccag	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt	120 180 240 300 360
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggccac gatatcaact	teteggteat acttegggge tgggcegggg tgeggegtet agaaaeteea ggetgagtgg atttggettt	gcgtgtggta caagcgctcg gtgcaagcgg gctgggccca atttggccag gtcaggtgtt	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag	120 180 240 300 360 420
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggcac gatatcaact tggtgagaat ccgtatgcc	teteggteat acttegggge tgggeeggg tgeggegtet agaaaeteea ggetgagtgg atttggettt egetgaatet	gcgtgtggta caagcgctcg gtgcaagcgg gctgggccca atttggccag gtcaggtgtt cctggctgac	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat	120 180 240 300 360 420 480
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggcac gatatcaact tggtgagaat ccgtatgccc gtgtgcactg ggcattataa	teteggteat acttegggge tgggeeggg tgeggegtet agaaaeteea ggetgagtgg atttggettt egetgaatet tggetettt	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt	120 180 240 300 360 420 480 540
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggcac gatatcaact tggtgagaat ccgtatgcc gtgtgcactg ggcattataa cattgatgca aatatggtgg	teteggteat acttegggge tgggeeggg tgeggegtet agaaaeteea ggetgagtgg atttggettt egetgaatet tggetettt	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tcttttctgt	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca	120 180 240 300 360 420 480 540
<211> 1621	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctcttt aaggaacagc cacctcgagg	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt	120 180 240 300 360 420 480 540 600
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggcac gatatcaact tggtgagaat ccgtatgccc gtgtgcactg ggcattataa cattgatgca aatatggtgg gaaatcgagt ctgtgggaag ctatacgact tacaggacag	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctctttt aaggaacagc cacctcgagg cagatggga	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tcttttctgt ttggatggtg gttggagcaa	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca	120 180 240 300 360 420 480 540 600 660 720
<211> 1621	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctcttt aaggaacagc cacctcgagg cagatggga aaggacttgg	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat	120 180 240 300 360 420 480 540 600 660 720 780
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt atttatgcca agctggcac gatatcaact ttggtgagaat ccgtatgcc gtgtgcactg ggcattataa cattgatgca aatatggtgg gaaatcgagt ctgtgggaag ctatacgact tacaggacag gttctacgag ctgctgatca gagcatggat gattggccag	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctctttt aaggaacagc cacctcgagg cagatggga aaggacttgg aaatgaagaa	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac	120 180 240 300 360 420 480 540 600 660 720 780 840
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt attatgcca agctggcac gatatcaact tggtgagaat ccgtatgccc gtgtgcactg ggcattataa cattgatgca aatatggtgg gaaatcgagt ctgtgggaag ctatacgac tacaggacag gttctacgag ctgctgatca gagcatggat gattggccag gaaggcagag tggtgtcaaa	teteggteat actteggge tgggceggg tgeggegtet agaaacteca ggetgagtgg atttggettt egetgaatet tggetettt aaggaacage cacetegagg cagatggga aaggaettgg aaatgaagaa tetttgaegg	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac	120 180 240 300 360 420 480 540 600 660 720 780 840 900
<211> 1621	teteggteat actteggge tgggceggg tgeggegtet agaaacteca ggetgagtgg atttggettt egetgaatet tggetettt aaggaacage cacetegagg cagatggga aaggaettgg aaatgagga atttgaegg attttgaegg atgateacaa	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc caaggaacgg	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc ggctcgttta	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac tcaccagtga	120 180 240 300 360 420 480 540 600 720 780 840 900 960
<211> 1621 <212> DNA <213> Homo sapie <400> 107 cgccatggca ctgcagggca ctgtgctatg gtcctggctg ccgctacgac gtgagccgct gccgcgggga gccgccgtgc cttccgccgc ggtgtcatgg tccaaggctt attatgcca agctggcac gatatcaact tggtgagaat ccgtatgccc gtgtgcactg ggcattataa cattgatgca aatatggtgg gaaatcgagt ctgtgggaag ctatacgac tacaggacag gttctacgag ctgctgatca gagcatggat gattggccag gaaggcagag tggtgtcaaa	teteggteat actteggge tgggceggg tgeggegtet agaaacteca ggetgagtgg atttggettt egetgaatet tggetettt aaggaacage cacetegagg cagatggga aaggaettgg aaatgagga atttgaegg attttgaegg atgateacaa	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc caaggaacgg	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc ggctcgttta	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac tcaccagtga	120 180 240 300 360 420 480 540 660 720 780 840 900 960 1020
<211> 1621	tctcggtcat acttcggggc tgggcgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctcttt aaggaacagc cacctcgagg cagatggga aaggacttgg aaatgaagaa tctttgacgg atgatcacaa gccctgcacc	gcgtgtggta caagcgctcg gtgcaagcgg gctgggccaa atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc caaggaacgg tctgctgtta	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc ggctcgttta aacaccccag	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac tcaccagtga ccatcccttc	120 180 240 300 360 420 480 540 600 720 780 840 900 960 1020 1080
<211> 1621	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctcttt aaggaacagc cacctcgagg cagatggga aaggacttgg aaatgaagaa tctttgacgg atgatcacaa gccctgcacc taggagaaca agcttaactc	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc caaggaacgg tctgctgtta cactgaggag agataaaatc	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc ggctcgttta aacaccccag atacttgaag attgaagta	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac tcaccagtga ccatcccttc aatttggatt ataaggtaaa	120 180 240 300 360 420 480 540 600 720 780 840 900 960 1020 1080 1140
<211> 1621	tctcggtcat acttcggggc tgggccgggg tgcggcgtct agaaactcca ggctgagtgg atttggcttt cgctgaatct tggctcttt aaggaacagc cacctcgagg cagatggga aaggacttgg aaatgaagaa tctttgacgg atgatcacaa gccctgcacc taggagaaca agcttaactc gcccacggct	gcgtgtggta caagcgctcg gtgcaagcgg gctgggcca atttggccag gtcaggtgtt cctggctgac tgaccgcaca atatttaagt acagaacatg attcatggct actaaagtct gaagtttgca cacagatgcc caaggaacgg tctgctgtta cactgaggag agataaaatc caagtgaatt	cgcgtggacc ctagtgctgg tcggatgtgc gagattctgc tcaggaagct ctctcaaaaa tttgctggtg cgcactgaca tctttctgt ttggatggtg gttggagcaa gatgaacttc gatgtatttg tgtgtgactc ggctcgttta aacaccccag atacttgaag attgaaagta tgaatactgc	ggcccggctc acctgaagca tgctggagcc agcgggaaaa tctgccggtt ttggcagaag gtggccttat agggtcaggt ggaaaactca gagcaccttt tagaacccca ccaatcagat caaagaagac cggttctgac tcaccagtga ccatcccttc aatttggatt ataaggtaaa atttacagtg	120 180 240 300 360 420 480 540 600 720 780 840 900 960 1020 1080

agt ttt att	ttati ttga: ttac:	tate tetg atgg acte	cct gtt ttg	aggg tcca ctag attc	ctt gtt tga ; tac ;	ttga tgct aaaa aatg	ttta tgat ggaa taga	ta a at a tg a aa a	aact tttg tata tqaq	ttgg ttga ttct qaaa	g ta t at t ga t gc	ctta taag agac caca	tact attc atcg	aaa ttg ata	ttctaaa ttatggt acttata tacattt tggtgat aaaaaaa
	<210> 108														
			> 382												
			> PR'												
	<	(213)	> HOI	no sa	apier	ì									
	<	400	> 108	3											
Met					/ Ile	Sei	r Val	Met	- Gly	1 T.A1	. 601	~ Cl-			a Pro
_				5					10					3 6	
Gly	Pro	Phe	e Cys	Ala	a Met	. Val	l Leu	ı Ala	a Ası) Phe	∍ Gly	/ Ala	Arc	r Val	l Val
			20					25					3.0		
Arg	val	. ASI	Arg	Pro	GIA	Ser	Arg	J Tyr	Asp	Val	l Ser		Leu	Gly	/ Arg
Gly	Lvs		ı Ser	Leu	Val	Lei	40 1 Acr	. T.o.	Lare		. D	45	a 1		a Ala
_	50	_	,			55	. 110£	, nec	. шуг	GII	. 60	Arg	Gly	Αlέ	a Ala
Val	Leu	Arg	J Arg	Leu	Cys	Lys	Arg	Ser	Asp	Va]	Leu	Leu	Glu	Pro	Phe
65					70					75					9.0
Arg	Arg	GIY	v Val	Met	Glu	Lys	Leu	Gln	Leu	Gly	Pro	Glu	Ile	Leu	Gln
Ara	Glu	Asr	Pro	85 Ara	T.011	Tlo		- N1 -	90	_				95	
5			100	9	neu	110	TÄT	105		Leu	Ser	Gly		Gly	Gln
Ser	Gly	Ser	Phe	Cys	Arg	Leu	Ala	Gly	His	Asn	Ile	Asn	110 Tyr	T.611	Ala
		TTO					120					125			
Leu	Ser	Gly	Val	Leu	Ser	Lys	Ile	Gly	Arg	Ser	Gly	Glu	Asn	Pro	Tyr
	130					135					140				
145	110	Dea	ASII	пец	150	Ala	Asp	Pne	Ala	G1y 155	Gly	Gly	Leu	Met	Cys
Ala	Leu	Gly	Ile	Ile		Ala	Leu	Phe	Asp	Ara	Thr	Ara	Thr	λαη	160 Lys
				165					170					175	
Gly	Gln	Val	Ile	Asp	Ala	Asn	Met	Val	Glu	Gly	Thr	Ala	Tyr	Leu	Ser
			TRO					185					190		
ber	FIIC	195	пр	гуѕ	IIII	GIN	Lys 200	Ser	Ser	Leu	Trp		Ala	Pro	Arg
Gly	Gln			Leu	Asp	Glv	Gly	Ala	Pro	Phe	ጥረታ	205	Thr	т	A
	210					215					220				
Thr	Ala	Asp	Gly	Glu	Phe	Met	Ala	Val	Gly	Ala	Ile	Glu	Pro	Gln	Phe
223					230					235					240
ıyı	GIU	reu	ьeu	11e 245	ьуs	Gly	Leu	Gly	Leu	Lys	Ser	Asp	Glu	Leu	Pro
Asn	Gln	Met	Ser		Asn	Δen	Trp	Dro	250	Mon	T	.		255	
			260					265					270		
Asp	Val	Phe	Ala	Lys	Lys	Thr	Lys	Ala	Glu	Trp	Cvs	Gln	Ile	Phe	Δςη
		2/5					280					285			
Gly	Thr	Asp	Ala	Cys	Val	Thr	Pro	Val	Leu	Thr	Phe	Glu	Glu	Val	Val
	290					295					300				
His 305		- - 20 P	****	usii	шуs 310	GIU	Arg	стА	ser	Phe	Ile	Thr	Ser	Glu	
Gln	Asp	Val	Ser	Pro		Pro	Ala	Pro	T.e.1	J.211	Lou	Nan	Th.	D	320

Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala

```
330
                325
                                                         335
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
                                345
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn
                            360
Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu
                        375
      <210> 109
      <211> 1524
      <212> DNA
      <213> Homo sapien
      <400> 109
ggcacgaggc tgcgccaggg cctgagcgga ggcgggggca gcctcgccag cgggggcccc
                                                                        60
gggcctggcc atgcctcact gagccagcgc ctgcgcctct acctcgccga cagctggaac
                                                                       120
cagtgegace tagtggctct cacctgcttc ctcctgggcg tgggctgccg gctgaccccg
                                                                       180
ggtttgtacc acctgggccg cactgtcctc tgcatcgact tcatggtttt cacggtgcgg
                                                                       240
ctgcttcaca tcttcacggt caacaaacag ctggggccca agatcgtcat cgtgagcaag
                                                                       300
atgatgaagg acgtgttctt cttcctcttc ttcctcggcg tgtggctggt agcctatggc
                                                                       360
gtggccacgg aggggctcct gaggccacgg gacagtgact tcccaagtat cctgcgccgc
                                                                       420
gtottotacc gtocotacct gcagatotto gggcagatto cccaggagga catggacgtg
                                                                       480
geocteatgg ageacageaa etgetegteg gagecegget tetgggeaca eceteetggg
                                                                       540
geocaggegg geacetgegt eteccagtat gecaactgge tggtggtget geteetegte
                                                                       600
atottectge tegtggeeaa cateetgetg gteaacttge teattgeeat gtteagttae
                                                                       660
acatteggea aagtacaggg caacagegat ctctactgga aggegeageg ttacegeete
                                                                       720
atcogggaat tocactotog geologogoty geologocot trategical choccactty
                                                                       780
egectectge teaggeaatt gtgeaggega ceeeggagee eecageegte eteceeggee
                                                                       840
ctcgagcatt tccgggttta cctttctaag gaagccgagc ggaagctgct aacgtgggaa
                                                                       900
teggtgcata aggagaactt tetgetggca egegetaggg acaageggga gagegaetee
                                                                       960
gagcgtctga agcgcacgtc ccagaaggtg gacttggcac tgaaacagct gggacacatc
                                                                      1020
cgcgagtacg aacagcgcct gaaagtgctg gagcgggagg tccagcagtg tagccgcgtc
                                                                      1080
ctggggtggg tggccgaggc cctgagccgc tctgccttgc tgcccccagg tgggccgcca
                                                                      1140
ccccctgacc tgcctgggtc caaagactga gccctgctgg cggacttcaa ggagaagccc
                                                                      1200
ccacagggga ttttgctcct agagtaaggc tcatctgggc ctcggccccc gcacctggtg
                                                                      1260
gccttgtcct tgaggtgagc cccatgtcca tctgggccac tgtcaggacc acctttggga
                                                                      1320
gtgtcatcct tacaaaccac agcatgcccg gctcctccca gaaccagtcc cagcctggga
                                                                      1380
ggatcaaggc ctggatcccg ggccgttatc catctggagg ctgcagggtc cttggggtaa
                                                                      1440
cagggaccac agacccctca ccactcacag attcctcaca ctggggaaat aaagccattt
                                                                      1500
cagaggaaaa aaaaaaaaaa aaaa
                                                                      1524
      <210> 110
      <211> 3410
      <212> DNA
      <213> Homo sapien
      <400> 110
gggaaccagc ctgcacgcgc tggctccggg tgacagccgc gcgcctcggc caggatctga
                                                                        60
gtgatgagac gtgtccccac tgaggtgccc cacagcagca ggtgttgagc atgggctgag
                                                                       120
aagctggacc ggcaccaaag ggctggcaga aatgggcgcc tggctgattc ctaggcagtt
                                                                       180
ggcggcagca aggaggagag gccgcagctt ctggagcaga gccgagacga agcagttctg
                                                                       240
                                                                       300
gagtgcctga acggccccct gagccctacc cgcctggccc actatggtcc agaggctgtg
ggtgagccgc ctgctgcggc accggaaagc ccagctcttg ctggtcaacc tgctaacctt
                                                                       360
tggcctggag gtgtgtttgg ccgcaggcat cacctatgtg ccgcctctgc tgctggaagt
                                                                       420
                                                                       480
gggggtagag gagaagttca tgaccatggt gctgggcatt ggtccagtgc tgggcctggt
```

~						
ctgtgtccc	g ctcctaggc	t cagccagtga	a ccactggcg	t ggacgctat	g gccgccgccg	540
gccccccac	u rgggcactgi	t ccttgggcat	t cctgctgag	d didtitions:	a teccaaggg	600
caaccaacc	a gcagggctg	- tgtgcccgga	a teceaggee	ctagaacta	Cactoctcat	660
cccaaacaci	a gggergerg	g acttetgtgg	g ccaggtqtqc	: ttcactccad	tagaaaccct	720
getetetga	- ctcttccgg	g acccggacca	a ctqtcqccac	gcctactctc	tctatocctt	780
caegaecagi	- crrgggggci	- gcctgggcta	a cctcctgcct	gccattgact	gggacaccag	840
rgecergge	- ccctacctg	y gcacccagga	a ggagtgcctc	: tttaacctaa	traccetest	900
CCCCCCCCCCCC	: rgcgtagcag	; ccacactgct	qqtqqctqac	a daddcadcad	tagacccasa	960
cgagecage	a gaayyyctgi	- cggcccctc	: cttatcaccc	: cactoctot	catoccooo	1020
cegeeegge	. LLCCggaacc	: rgggcgccct	getteedaa	, ctgcaccago	tatactacca	1080
catgetteg	accetgege	ggetettegt	ggctgagctc	: tacaactaaa	taggactcat	1140
gaccccac	, crarritace	cggatttcqt	qqqcqaqqq	, ctgtaccacc	acatacaca	1200
agergageeg	, ggcaccgagg	, cccggaqaca	i Ctatqatqaa	l gacattcaaa	tagacagast	1260
aaaaccacc	. ctgcagtgcg	, ccatctccct	gatettetet	ctaatcatac	1 accordtest	1320
geagegatte	. ggcactcgag	cagtetattt	gaccaatata	r gcagetttee	ctataaataa	1380
cggcgccaca	regoongreed	acagtgtggc	: cataataaca	getteageed	ccctcacccc	1440
geecaceeee	. ccagecerge	agatectqce	: Ctacacacto	geeteetet	200200000	1500
gaagcaggeg	Lectigodda	aataccgagg	ggacactgga	ggtgctagca	atasaasas	1560
cergargace	agettettge	cayyccctaa	geetggaget	- cccttcccta	atogacacat	1620
3335365334	ggcagiggco	rgereceace	tccacccaca	- etetacaaaa	CCTCTGCGTG	1680
egal.gccccc	gracgrargg	rggrgggrga	gcccaccgag	accadantaa	ttccaaaaa	1740
gggcaccigc	crygacereg	ccatcctgga	tagtgccttc	ctactatece	aggtageeee	1800
accettget	argygereca	ttgtccagct	cagocaqtot	gtcactgcct	atatootoro	1860
raccacagge	cigggicigg	regecattta	ctttqctaca	caggtagtat	ttgacaagag	1920
egacteggee	adatactcag	cgtagaaaac	ttccaqcaca	ttagaataaa	adacet acet	1980
cactgggttt	cagereeeeg	ctcctgttag	ccccatagaa	ctaccaaact	aaccacaaat	2040.
ceeegeegee	gccaaagtaa	tgtggctctc	tactaccacc	ctatactact	gaggt gggt a	2100
geegeacage	rgggggcrgg	ggcgtccctc	tectetetee	ccagteteta	ggggtgggg	2160
accagaagacc	ccccaagggg	gulleagtet	ggacttatac	auccaaaacca	gaaggggtgg	2220
argeacryga	argeggggae	tctgcaggtg	gattacccag	gctcagggtt	aacadet age	2280
ceceageeg	agacacaccc	agagaagggt	ttttqqqaqc	tgaataaact	cagtraceto	2340
gereceare	cctaageeee	ttaacctgca	gcttcgttta	atgtagetet	tacataggaa	2400
ccccaggat	gaaacactcc	tccatgggat	ttgaacatat	gacttatttg	taggggaaga	2460
geeeegaggg	gcaacacaca	agaaccaqqt	CCCCtcagcc	Cacaggagto	totttttaat	2520
gatteatte	CCCCCCaccc	LLLatcagga	tataacctat	tagtccttct	attaccetae	2580
cagagacaca	ggcacttaaa	Lalttaactt	atttatttaa	Caaagtagaa	gggaatggat	2640
egetagettt	tergrating	Lycctaatat	ttaaataaaa	tagaggatcc	CCAACAAFGA	2700
ggccccctga	garagergge	cattgggctg	atcattocca	gaatcttctt	ctcctagaat	2760
crageceeee	addatyccta	acccaggacc	ttggaaattc	tactcatccc	aaatrataat	2820
cccaaacycc	grracecaag	grragggtgt	tgaaggaagg	tagagggtag	aaattaa	2880
cccaacggc	Lecctaacca	cccctcttct	Cttggcccag	cctggttccc	CCCacttaga	2940
CCCCCCCC	ciclectag	gactgggctg	atgaaggcac	tocccaaaar	ttcccctacc	3000
CCCaactttt	CCCLaccccc	aactttcccc	accageteca	caaccctott	togagetact	3060
geaggaceag	aaycacaaag	racaarrec	caageettta	tccatctcac	CCCCCacact	3120
atatctgtgc	ttggggaatc	tcacacagaa	actcaggage	acccctacc	tgaggtaagg	
gaggictiat	ccccagggg	gggtttaagt	gccgtttgca	ataatgtcgt	Cttatttatt	3180
cagegggggg	aatatttat	actgtaagtg	agcaatcaga	gtataatgtt	tatootoaca	3240
aaattaaagg	ctttcttata	tgtttaaaaa	aaaaaaaaa	aaaaaaaaaa	aaaaaaaaa	3300
aaaaaaara	aaaaaaaaa	aaaaaaaaa	aaaaaaataa	aaaaaaaaa	uuuuaaaaaa	3360
						3410

<210> 111

<211> 1289

<212> DNA

<213> Homo sapien

<400> 111 agccaggcgt ccctctgcct gcccactcag tggcaacacc cgggagctgt tttgtccttt 60 gtggagcctc agcagttccc tctttcagaa ctcactgcca agagccctga acaggagcca 120 ccatgcagtg cttcagcttc attaagacca tgatgatcct cttcaatttg ctcatcttc 180 tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcatcctttc 240 tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc 300 tcatcgcagc cggcgttgtg gtctttgctc ttggtttcct gggctgctat ggtgctaaga 360 ctgagagcaa gtgtgccctc gtgacgttct tcttcatcct cctcctcatc ttcattgctg 420 aggttgcagc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480 tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt 540 ggaacaccac catgaaaggg ctcaagtgct gtggcttcac caactatacg gattttgagg 600 actcacccta cttcaaagag aacagtgcct ttcccccatt ctgttgcaat gacaacgtca 660 ccaacacage caatgaaace tgcaccaage aaaaggetca egaccaaaaa gtagagggtt 720 gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag 780 ctggaattgg gggcctcgag ctggctgcca tgattgtgtc catgtatctg tactgcaatc 840 tacaataagt ccacttctgc ctctgccact actgctgcca catgggaact gtgaagaggc 900 accetggcaa geageagtga ttgggggagg ggaeaggate taacaatgte acttgggeea 960 gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg 1020 atgcctgact ttccttccat tggtgggtgg atgggtggg ggcattccag agcctctaaq 1080 gtagccagtt ctgttgccca ttcccccagt ctattaaacc cttgatatgc cccctaggcc 1140 tagtggtgat cccagtgctc tactggggga tgagagaaag gcattttata gcctgggcat 1200 aagtgaaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260 tgttacaatg ttaaaaaaaa aaaaaaaaa 1289

<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln 5 10 Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala 40 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu 55 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro 75 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser 90 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys 100 105 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe 120 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe 140 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys 150 155 160 Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu 165 170 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln 185 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

195 200 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr 215 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp 230 235 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val 245 250 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly 280 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly 295 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp 305 310

<210> 113

<211> 553

<212> PRT

<213> Homo sapien

<400> 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala Gln Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu 25 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly 55 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu 105 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly 120 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu 135 140 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala 150 155 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr 165 170 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu 185 Gly Thr Gln Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu 200 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly 215 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His 230 235 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg

			260					265					270		
Arg	Leu	Phe	Val	Ala	Glu	Leu	Cys	Ser	Trp	Met	Ala	Leu	Met	Thr	Phe
		275					280					285			
Thr	Leu	Phe	Tyr	Thr	Asp	Phe	Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val
	290					295					300				
Pro	Arg	Ala	Glu	Pro	Gly	Thr	Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly
305					310					315					320
Val	Arg	Met	Gly	Ser	Leu	Gly	Leu	Phe	Leu	Gln	Cys	Ala	Ile	Ser	Leu
				325					330					335	
Val	Phe	Ser	Leu	Val	Met	Asp	Arg	Leu	Val	Gln	Arg	Phe	Gly	Thr	Arg
			340					345					350		
Ala	Val	Tyr	Leu	Ala	Ser	Val	Ala	Ala	Phe	Pro	Val	Ala	Ala	Gly	Ala
		355					360					365			
Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
	370					375					380				
Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr	Leu	Ala
385					390					395					400
Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val		Leu	Pro	Lys	Tyr	Arg	Gly
				405					410					415	
Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu
			420					425					430		
Pro	Gly	Pro	Lys	Pro	Gly	Ala		Phe	Pro	Asn	Gly	His	Val	Gly	Ala
		435					440					445			
Gly	Gly	Ser	Gly	Leu	Leu		Pro	Pro	Pro	Ala		Cys	Gly	Ala	Ser
	450					455					460				
	Cys	Asp	Val	Ser		Arg	Val	Val	Val		Glu	Pro	Thr	Glu	
465					470			•		475		_			480
Arg	Val	Val	Pro	_	Arg	Gly	Ile	Cys		Asp	Leu	Ala	Ile		Asp
		_		485	_				490	_				495	_
Ser	Ala	Phe		Leu	Ser	Gln	Val		Pro	Ser	Leu	Phe		Gly	Ser
			500	_		_		505		_			510		
Ile	Val		Leu	Ser	GIn	Ser		Thr	Ala	Tyr	Met		Ser	Ala	Ala
		515	_				520					525			_
Gly	Leu	Gly	Leu	Val	Ala		Tyr	Phe	Ala	Thr		Val	Val	Phe	Asp
_	530	_	_		_	535	_				540				
-	Ser	Asp	Leu	Ala	-	ıyr	Ser	Ala							
545					550										

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

 Met
 Gln
 Cys
 Phe
 Ser
 Phe
 Ile
 Lys
 Thr
 Met
 Met
 Ile
 Leu
 Phe
 Asn
 Leu

 1
 1
 5
 2
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1
 1

WO 00/04149 PCT/US99/15838

```
85
                                      90
                                                           95
 Phe Ile Ala Glu Val Ala Ala Val Val Ala Leu Val Tyr Thr Thr
                                  105
                                                      110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
         115
                              120
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
                          135
                                              140
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
                     150
                                          155
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
                                      170
                                                          175
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
                                  185
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
                             200
                                                  205
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
                         215
                                              220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
 225
                     230
                                         235
                                                              240
Gln
       <210> 115
       <211> 366
       <212> DNA
       <213> Homo sapien
       <400> 115
gctctttctc tcccctcctc tgaatttaat tctttcaact tgcaatttgc aaggattaca
                                                                         60
catttcactg tgatgtatat tgtgttgcaa aaaaaaaaa gtgtctttgt ttaaaattac
                                                                        120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                        180
actggtagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                        240
tctcagaacc atttcaccca gacagcctgt ttctatcctg tttaataaat tagtttgggt
                                                                        300
tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt
                                                                        360
ttagtc
                                                                        366
      <210> 116
      <211> 282
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(282)
      <223> n = A,T,C or G
      <400> 116
acaaagatga accatttcct atattatagc aaaattaaaa tctacccgta ttctaatatt
                                                                        60
gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa
                                                                       120
agactttact attttcatat tttaagacac atgatttatc ctattttagt aacctggttc
                                                                       180
atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt
                                                                       240
tcaatcinga actaictana tcacagacat tictaitcci ti
                                                                       282
      <210> 117
      <211> 305
```

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(305)
      <223> n = A,T,C or G
      <400> 117
acacatqtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca
                                                                         60
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa
                                                                         120
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga
                                                                         180
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt
                                                                         240
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat
                                                                         300
                                                                         305
tgggt
      <210> 118
      <211> 71
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(71)
      <223> n = A, T, C \text{ or } G
      <400> 118
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa
                                                                          60
                                                                          71
aantcctggg t
      <210> 119
      <211> 212
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(212)
      <223> n = A, T, C or G
      <400> 119
actecqqttq qtqtcaqcaq cacqtggcat tqaacatngc aatgtggagc ccaaaccaca
                                                                          60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac
                                                                         120
aqtaaqctgg cccttctaat aaaagaaaat tgaaaggttt ctcactaanc ggaattaant
                                                                         180
aatggantca aganactccc aggcctcagc gt
                                                                         212
      <210> 120
      <211> 90
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(90)
      <223> n = A, T, C or G
```

```
<400> 120
actogttgca nateagggge cocceagagt cacegttgca ggagteette tggtettgee
                                                                          60
 ctccgccggc gcagaacatg ctggggtggt
                                                                          90
       <210> 121
       <211> 218
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(218)
       <223> n = A,T,C or G
       <400> 121
 tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcatttga
                                                                         60
 gaataagatt tgctaaaaga tttggggcta aaacatggtt attgggagac atttctgaag
                                                                        120
 atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc
                                                                        180
 agcatanact tcatgtgggg atancagcta cccttgta
                                                                        218
       <210> 122
       <211> 171
       <212> DNA
       <213> Homo sapien
       <400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg
                                                                         60
catttgttag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt
caccaccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t
                                                                        120
                                                                        171
       <210> 123
       <211> 76
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (76)
      <223> n = A,T,C or G
      <400> 123
tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca
                                                                        60
ttatcaanta ttgtgt
                                                                         76
      <210> 124
      <211> 131
      <212> DNA
      <213> Homo sapien
      <400> 124
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt
                                                                        60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg
                                                                       120
ttaagatttg t
                                                                       131
```

```
<210> 125
      <211> 432
      <212> DNA
      <213> Homo sapien
      <400> 125
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg
                                                                        60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa
                                                                       120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat
                                                                       180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg
                                                                       240
ctcttqaaqt atcaqtcact tttgagaatg tttcttagtt actgcatact tcatqqatcc
                                                                       300
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaatctcag
                                                                       360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc
                                                                       420
ctctttgctt gt
                                                                       432
      <210> 126
      <211> 112
      <212> DNA
      <213> Homo sapien
      <400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat
                                                                        60
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt
                                                                       112
      <210> 127
      <211> 54
      <212> DNA
      <213> Homo sapien
      <400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaagcaca gcag
                                                                        54
      <210> 128
      <211> 323
      <212> DNA
      <213> Homo sapien
      <400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc
                                                                        60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca
                                                                       120
ttctctctga agtctaggtt acccattttg gggacccatt ataggcaata aacacagttc
                                                                       180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt
                                                                       240
tteetgeaaa aggeteaete agteeettge ttgeteagtg gaetgggete eecagggeet
                                                                       300
aggetgeett etttteeatg tee
                                                                       323
      <210> 129
      <211> 192
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (192)
      <223> n = A,T,C or G
```

```
<400> 129
 acatacatgt gtgtatattt ttaaatatca cttttgtatc actctgactt tttagcatac
                                                                          60
 tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc
                                                                         120
 tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg
                                                                         180
 gataaacaaa qt
                                                                         192
       <210> 130
       <211> 362
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(362)
       <223> n = A, T, C or G
       <400> 130
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca
                                                                         60
tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa
                                                                         120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa
                                                                         180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata
                                                                         240
cttatttaaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat
                                                                         300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaatctta aaaagtaatg
                                                                        360
gg
                                                                        362
       <210> 131
       <211> 332
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
      <222> (1) ... (332)
      <223> n = A,T,C or G
      <400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca
                                                                         60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga
                                                                        120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc
                                                                        180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa
                                                                        240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc
                                                                        300
atanaaggat tgggtgaagc tggcgttgtg gt
                                                                        332
      <210> 132
      <211> 322
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(322)
      <223> n = A, T, C or G
      <400> 132
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctcctgaaaa ctaggtgtcc
                                                                        60
```

```
aqtqqctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat
                                                                         120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt
                                                                         180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg
                                                                         240
                                                                         300
qqatqcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct
                                                                         322
qtaacaatct acaattggtc ca
      <210> 133
      <211> 278
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(278)
      \langle 223 \rangle n = A,T,C or G
      <400> 133
acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt
                                                                          60
cttqtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta
                                                                         120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg
                                                                         180
ctattcctqt tttqtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt
                                                                         240
                                                                         278
cccacqaaac actaataaaa accacagaga ccagcctg
      <210> 134
      <211> 121
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(121)
      \langle 223 \rangle n = A,T,C or G
      <400> 134
gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta ttttaaaaca
                                                                          60
tgattctctq aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg
                                                                         120
                                                                         121
      <210> 135
      <211> 350
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(350)
      <223> n = A,T,C or G
      <400> 135
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc
                                                                          60
atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc
                                                                         120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca
                                                                         180
gggtgccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct
                                                                         240
ccacctcaat caagecetgg gecatgetac etgeaattgg etgaacaaac gtttgetgag
                                                                         300
                                                                         350
ttcccaagga tgcaaagcet ggtgctcaac tcctggggcg tcaactcagt
```

```
<210> 136
        <211> 399
        <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(399)
       <223> n = A,T,C or G
       <400> 136
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt
                                                                          60
 gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga
                                                                         120
                                                                         180
 cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag
                                                                         240
 aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc
 teccaggaac eegggeaaag gecateeeca eetacageea geatgeecae tggegtgatg
                                                                         300
                                                                         360
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt
                                                                         399
       <210> 137
       <211> 165
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(165)
       <223> n = A,T,C or G
       <400> 137
actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt
                                                                          60
ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga
                                                                         120
ttggctggtc ccactggtgg tcactgtcat tggtggggtt cctgt
                                                                         165
      <210> 138
      <211> 338
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(338)
      \langle 223 \rangle n = A,T,C or G
      <400> 138
actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc
                                                                         60
ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa
                                                                        120
tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg
                                                                        180
tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt
                                                                        240
cangcetcag gaageetcaa gtteeattea getttgeeae tgtacattee ecatntttaa
                                                                        300
aaaaactgat gccttttttt tttttttttg taaaattc
                                                                        338
      <210> 139
      <211> 382
```

```
<212> DNA
      <213> Homo sapien
      <400> 139
gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa
                                                                         60
gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga
                                                                        120
                                                                        180
attcaaacaq acctcgtcat tcctggtgtg agcctggtcg gctcaccgcc tatcatctgc
                                                                        240
atttqcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg
ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat
                                                                        300
gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg
                                                                        360
gcctggaact tgtttaaagt gt
                                                                        382
      <210> 140
      <211> 200
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(200)
      <223> n = A,T,C or G
      <400> 140
accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat
                                                                         60
acttttcatt taacancttt tgttaagtgt caggctgcac tttgctccat anaattattg
                                                                        120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt
                                                                        180
                                                                        200
atattcagca taaaggagaa
      <210> 141
      <211> 335
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (335)
      <223> n = A,T,C \text{ or } G
      <400> 141
                                                                          60
actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt
                                                                         120
atgcatgtag agaacccaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga
                                                                         180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg
                                                                         240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg
                                                                         300
                                                                         335
attcacaaac caagtaattt taaacaaaga cactt
       <210> 142
       <211> 459
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(459)
       <223> n = A, T, C \text{ or } G
```

```
<400> 142
 accaggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta
                                                                          60
 gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca
                                                                         120
 cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc
                                                                         180
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca
                                                                         240
                                                                         300
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga
                                                                         360
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct
                                                                         420
 cagcangggt gggaggaacc agctcaacct tggcgtant
                                                                         459
       <210> 143
       <211> 140
       <212> DNA
       <213> Homo sapien
       <400> 143
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag
                                                                         60
                                                                        120
 accatecgae tteectgtgt
                                                                        140
       <210> 144
       <211> 164
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(164)
       <223> n = A,T,C or G
      <400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct
                                                                         60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg
                                                                        120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt
                                                                        164
      <210> 145
      <211> 303
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(303)
      <223> n = A,T,C or G
      <400> 145
acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa
                                                                        60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat
                                                                       120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca
                                                                       180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat
                                                                       240
                                                                       300
caa
                                                                       303
```

<210> 146

```
<211> 327
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(327)
      <223> n = A,T,C or G
      <400> 146
actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac
                                                                        60
actqqcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct
                                                                       120
ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt
                                                                       180
cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc
                                                                       240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg
                                                                       300
taggggtgag ctgtgtgact ctatggt
                                                                       327
      <210> 147
      <211> 173
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ...(173)
      <223> n = A,T,C or G
      <400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg
                                                                        60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                       120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt
                                                                       173
      <210> 148
      <211> 477
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (477)
      <223> n = A, T, C or G
      <400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct
                                                                        60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact
                                                                       120
qccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg
                                                                       180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac
                                                                       240
nccancecae etcacegaee ecateetett acacagetae etcettgete tetaacecea
                                                                       300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag
                                                                       360
caccactggt aagcettete cagecaacae acacacae acacneacae acacacatat
                                                                        420
                                                                       477
ccaqqcacaq qctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg
      <210> 149
```

<211> 207

<212> DNA

WO 00/04149

```
<213> Homo sapien
        <400> 149
 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac
 taacgtattt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct
                                                                          60
 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca
                                                                          120
 tttcaggcag agggaacagc agtgaaa
                                                                         180
                                                                          207
       <210> 150
       <211> 111
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(111)
       <223> n = A,T,C \text{ or } G
       <400> 150
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t
                                                                          60
                                                                         111
       <210> 151
      <211> 196
      <212> DNA
      <213> Homo sapien
      <400> 151
agcgcggcag gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat
                                                                         60
ggataccaac cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag
                                                                         120
                                                                        180
gtgcatccgg ctcagt
                                                                        196
      <210> 152
      <211> 132
      <212> DNA
      <213> Homo sapien
      <400> 152
acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagaac
cttccccttt tcatctagtg gtggaaacct gatgctttat gttgacagga atagaaccag
                                                                         60
gagggagttt gt
                                                                        120
                                                                       . 132
      <210> 153
      <211> 285
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(285)
```

acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag

BNSDOCID: <WO__0004149A2_I_>

<223> n = A,T,C or G

<400> 153

```
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga
                                                                       120
qcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac
                                                                       180
cctqqctaqt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca
                                                                       240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt
                                                                       285
      <210> 154
      <211> 333
      <212> DNA
      <213> Homo sapien
      <400> 154
accacagtee tgttgggeea gggetteatg accetttetg tgaaaageea tattateace
                                                                        60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac
                                                                       120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg
                                                                       180
attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctgatttg
                                                                       240
aqtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggaqaatg
                                                                       300
gtcaggcctg tctcatccat atggatcttc cgg
                                                                       333
      <210> 155
      <211> 308
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(308)
      <223> n = A,T,C or G
      <400> 155
actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg
                                                                        60
gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat
                                                                       120
ttgaatcacg gtgcatacaa actotootgc ctgctcotcc tgggccccag ccccagcccc
                                                                       180
atcacagete actgetetgt teatecagge ceageatgta gtggetgatt ettettgget
                                                                       240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg
                                                                       300
                                                                       308
gccctggt
      <210> 156
      <211> 295
      <212> DNA
      <213> Homo sapien
      <400> 156
accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta
                                                                        60
ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga
                                                                       120
gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgcct cattctatgt
                                                                       180
ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat
                                                                       240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat
                                                                       295
      <210> 157
      <211> 126
      <212> DNA
      <213> Homo sapien
      <400> 157
                                                                        60
acaagtttaa atagtgctgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct
```

```
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc
                                                                         120
 cttagt
                                                                         126
       <210> 158
       <211> 442
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(442)
       <223> n = A,T,C or G
       <400> 158
acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg
                                                                         60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt
                                                                         120
gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt
                                                                        180
ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttggggatcc cagtgaagta
                                                                        240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggtg
                                                                        300
ccaaccetgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga
                                                                        360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg
                                                                        420
tgttcattct ctgatgtcct gt
                                                                        442
      <210> 159
      <211> 498
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(498)
      <223> n = A,T,C \text{ or } G
      <400> 159
acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc
                                                                         60
tccaacaaga actgaggttg cagagcgggt agggaagagt gctgttccag ttgcacctgg
                                                                        120
gctgctgtgg actgttgttg attcctcact acggcccaag gttgtggaac tggcanaaag
                                                                        180
gtgtgttgtt gganttgagc tcgggcggct gtggtaggtt gtgggctctt caacaggggc
                                                                        240
tgctgtggtg ccgggangtg aangtgttgt gtcacttgag cttggccagc tctggaaagt
                                                                        300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa
                                                                        360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn
                                                                        420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc
                                                                        480
aagggaataa gctgtggt
                                                                        498
      <210> 160
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(380)
      <223> n = A, T, C or G
      <400> 160
```

acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac	60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct	120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc	180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc	240
ccaccettae etceatetea cacacttgag etttecaete tgtataatte taacateetg	300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa	360
cttgtagaat gaagcctgga	380
<210> 161	
<211> 114	
<212> DNA	
<213> Homo sapien	
·	
<400> 161	
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca	60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt	114
<210> 162	
<211> 177	
<212> DNA	
<213> Homo sapien	
<400> 162	
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa	60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt	120
tggtgatata taacttggca ataacccagt ctggtgatac ataaaactac tcactgt	177
<210> 163	
<211> 137	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc feature	
<222> (1)(137)	
<223> n = A,T,C or G	
<400> 163	
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac	60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagegge atgatgt	137
<210> 164	
<211> 469	
<212> DNA	
<213> Homo sapien	
Table 1.0mo bupaci.	
<220>	
<221> misc_feature	
<222> (1)(469)	
<223> n = A,T,C or G	
1222 11 - 11, 1, 0 01 0	
<400> 164	
cttatcacaa tgaatgttet eetgggeage gttgtgatet ttgeeacett egtgaettta	60
tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaccaggaaa	120

```
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt
                                                                         180
 gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg
                                                                         240
 ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg
                                                                         300
 gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct
                                                                         360
 tctagtaggc acagggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat
                                                                         420
 gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt
                                                                         469
       <210> 165
       <211> 195
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(195)
       <223> n = A,T,C or G
       <400> 165
acagtttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctggtgg
                                                                         60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc
                                                                        120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact
                                                                        180
tcctctgaga tgagt
                                                                        195
       <210> 166
       <211> 383
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A,T,C or G
      <400> 166
acatettagt agtgtggcae atcaggggge cateagggte acagteacte atageetege
                                                                         60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct
                                                                        120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt
                                                                        180
tttgcagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcaggtg
                                                                       240
gatgccaacc tegtetangg teegtgggaa getggtgtee aenteaceta caacetggge
                                                                       300
gangatetta taaagagget eenagataaa etecaegaaa ettetetggg agetgetagt
                                                                       360
nggggccttt ttggtgaact ttc
                                                                       383
      <210> 167
      <211> 247
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(247)
      <223> n = A,T,C or G
      <400> 167
acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat
                                                                        60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc
                                                                       120
```

tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag a tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgangtc	
<210> 168 <211> 273 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(273) <223> n = A,T,C or G	
<pre><400> 168 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg t aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt t gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag t aattcccaac ttccttgcca caagcttccc aggctttctc ccctggaaaa c agtcccagat acactcatgg gctgccctgg gca</pre>	tccacaaagg 120 tagggtgggc 180
<210> 169 <211> 431 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(431) <223> n = A,T,C or G	
<pre><400> 169 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tagctcagacc agggtcaaag gatgtgacat caacagtttc tggtttcaga ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg ggcagcagaa agggggtant tactgatgga caccatcttc tctgtatact cttgccatgg gcaaaaggccc ctaccacaaa aacaatagga tcactgctgg acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac aaagtgatct gatactggat tcttaattac cttcaaaaagc ttctgggggc tcgaacactg a</pre>	acaggttcta 120 cacaggtgag 180 ccacactgac 240 gcaccagctc 300 atccaactgg 360
<210> 170 <211> 266 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(266) <223> n = A,T,C or G	
<400> 170 acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca tcaaggagct ctgcaggcat tttgccaanc ctctccanag canagggagc ccccgctaga aagacaccag attggagtcc tgggaggggg agttggggtg	aacctacact 120

```
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct
                                                                        240
 tcaaagctag gggtctggca ggtgga
                                                                        266
       <210> 171
       <211> 1248
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(1248)
       <223> n = A, T, C or G
       <400> 171
 ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca
                                                                         60
 ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg
                                                                        120
 tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg
                                                                        180
 cacagtettg aggeegacca agageeaggg ageeagatgg tggaggeeag ceteteegta
                                                                        240
 cggcacccag agtacaacag accettgete getaacgace teatgeteat caagttggae
                                                                        300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc
                                                                        360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc
                                                                        420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac
                                                                        480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc
                                                                        540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc
                                                                        600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc
                                                                        660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa
                                                                       720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct
                                                                       780
ccctcaggcc caggagtcca ggcccccagc ccctcctccc tcaaaccaag ggtacagatc
                                                                       840
cccagcccct cctccctcag acccaggagt ccagacccc cagcccctcc tccctcagac
                                                                       900
ccaggagtcc ageceetect eceteagace caggagteca gaeceeceag eceetectee
                                                                       960
ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc
                                                                      1020
ccaaccente attecceaga eccagaggte caggteccag eccetentee etcagaccea
                                                                      1080
geggtecaat gecaectaga etntecetgt acacagtgee ecettgtgge aegttgaece
                                                                      1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt
                                                                      1200
aagagaagng caaaaaaaa aaaaaaaaa aaaaaaaaa
                                                                      1248
      <210> 172
      <211> 159
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(159)
      <223> Xaa = Any Amino Acid
      <400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
                 5
                                    10
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
                                25
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
                            40
                                                45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
    50
                        55
```

120

180

240

300

360

420

480

540 600

660

720

780

840 900

960

1020

1080

1140

1200 1260

1265

```
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
                                         75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
                                    90
                85
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
                                105
            100
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
                                                 125
                            120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
                                             140
                        135
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                                         155
145
      <210> 173
      <211> 1265
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (1265)
      <223> n = A, T, C \text{ or } G
      <400> 173
qqcaqcccqc actcgcagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc
tegggegtee tggtgcatee geagtgggtg etgteageeg caeaetgttt eeagaactee
tacaccatcq qqctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc
attgcttcgc agtgccctac cgcggggaac tcttgcctcg tttctggctg gggtctgctg
gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca
qcatqttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg
ggcccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag
tocaggecce cagecettee teecteaaac caagggtaca gateeccage ceeteeteec
tcagacccag gagtccagac cccccagccc ctcctccctc agacccagga gtccagcccc
tecteentea gacceaggag tecagaceee ceageceete eteceteaga eecaggggtt
qaqqcccca accctcctc cttcagagtc agaggtccaa gcccccaacc cctcgttccc
```

cagacccaga ggtnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc

tagattttcc ctgnacacag tgcccccttg tggnangttg acccaacctt accagttggt

ttttcatttt tnqtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa

<210> 174 <211> 1459

aaaaa

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1459)

<223> n = A,T,C or G

<400> 174

WO 00/04149

```
ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggcc
                                                                        60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg
                                                                       120
tacggcaccc agagtacaac agacccttgc tcgctaacga cctcatgctc atcaagttgg
                                                                       180
acgaatccgt giccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcccta
                                                                       240
ccgcggggaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg
                                                                       300
gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct
                                                                       360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga
ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg
                                                                       420
agggcaagac cagaaggact cctgcaacgt gagagaggg aaaggggagg gcaggcgact
                                                                       480
                                                                       540
cagggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag
                                                                       600
atggagagac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa
                                                                       660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggt
                                                                       720
gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa
                                                                       780
                                                                       840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt
tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc
                                                                       900
                                                                       960
gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga
                                                                      1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt
                                                                      1080
gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa
                                                                      1140
aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt
                                                                      1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg
                                                                      1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt
                                                                     1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt
                                                                     1380
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct
                                                                     1440
Caaaaaaaaa aaaaaaaaa
                                                                     1459
```

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1167)

<223> n = A,T,C or G

<400> 175

gcgcagccct	ggcaggcggc	actootoato	~~~~~~·			
ataastaas	3304330390	uccygicaly	gaaaacgaat	tgttctgctc	gggcgtcctg	60
gracuccyc	agtgggtgct	greageegea	cactotttcc	agaactccta	Caccatocca	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	accadataat	ggaggccagc	
ctctccqtac	ggcacccaga	gtacaacaca	CtCttcctcc	geeagaegge	ggaggccagc	180
aagttggacg	22100010		cicligateg	ctaacgacct	catgctcatc	240
aageeggaeg	aaccegegee	cgagtctgac	accatccgga	gcatcagcat	tacttacasa	300
egeceaccg	cggggaactc	Ligectegen	tetaaetaaa	atctactacc	Gaacgggaaa	
atgcctaccg	tgctgcactg	cgtgaacgtg	traataatat	atanaan-	gaacggcaga	360
CtCtatgacc	Cactatacaa	22222222	coggrage	ccgaggangt	ctgcagtaag	420
Zont one	cyclylacca	ccccagcatg	ttetgegeeg	gcggagggca	agaccagaaq	480
gaccccigca	acggrgacic	raaaaaaaccc	ctgatctgca	acqqqtactt	acagggggtt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	Cttagcatac	Caddtatata	50455500000	
tgcaaattca	Ctgagtggat	3030333300	at against	caggigicia	Caccaacctc	600
300001	there	agagaaaacc	greeagneea	gttaactctg	gggactggga	660
acceatgaaa	rigacececa	aatacatcct	gcqqaanqaa	ttcaggaata	totattagas	720
gcccctcctc	cctcaggccc	aggagtccag	gccccaacc	cctcctccct	G222G22	
gtacagatco	ccagcccctc	Ctccctcaca	GGGGGGGG		caaaccaagg	780
CCDtcacac	727700000	ctccctcaga	cccaggagtc	cagacccccc	agcccctcnt	840
cenceagace	cayyagtcca	gcccctcctc	cntcagacgc	aggagtccag	accccccage	900
				_		200

cententecg teagacecag gggtgeagge ecceaacece tenteentea gagteagagg tecaagece caaceceteg treecagae ecagaggtne aggreeage eccteeree teagacecag eggreeaarg ceacetagan threectgra cacagragece ectrograme eccetedee agreeage acetraceag transported extra ext	960 1020 1080 1140 1167
<pre><400> 176 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp</pre>	
1 5 10 15	
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu 20 25 30	
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val	
35 40 45 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu 50 55 60	
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser 65 70 75 80	
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly	
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met 100 105 110	
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val	
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala	
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly	
145 150 155 160 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys	
165 170 17 5	
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys 180 185 190	
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser 195 200 205	
<210> 177 <211> 1119 <212> DNA <213> Homo sapien <400> 177	
qcqcactcgc agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc	60
gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc	120 180
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg	240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct	300

420

480

540

600

660

720

780

840

900

960 1020

1080

1119

WO 00/04149

```
tegeagtgee ctacegeggg gaactettge etegtttetg getggggtet getggegaac
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc
 caaccetgge agggttgtac cattteggea acttecagtg caaggaegte etgetgeate
 ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc
 cagttateet caetgaattg agattteetg etteagtgte agecatteee acataattte
 tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa
 ttcatttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca
 ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg
 ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca
 accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg
 gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc
 ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa
       <210> 178
       <211> 164
       <212> PRT
       <213> Homo sapien
       <220>
       <221> VARIANT
       <222> (1)...(164)
       <223> Xaa = Any Amino Acid
       <400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
                                     10
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                                 25
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
                            40
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
                        55
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
                                         75
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
                                    90
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
                                105
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
                            120
                                                125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
                        135
                                            140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
                    150
                                        155
                                                            160
Pro Gly Thr Leu
```

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga ccagctgccc ccggccgggg gatgcgaggc tcggagcacc gccaggcact gttcatctca gcttttctgt ccctttgctc aagttcatat ctggagcctg atgtcttaac gaataaaggt aaaaaaaaaa	cttgcccggc ccggcaagcg	tgtgattgct cttctgctga	60 120 180 240 250
<210> 180 <211> 202 <212> DNA <213> Homo sapien			
<400> 180 actagtccag tgtggtggaa ttccattgtg ttgggcccaa tcacccagac cccgcccctg cccgtgcccc acgctgctgc ctctgctact cggaaactat ttttatgtaa ttaatgtatg tgatttaaaa aaaaaaaaaa	taacgacagt	atgatgctta	60 120 180 202
<210> 181 <211> 558 <212> DNA <213> Homo sapien			
<220> <221> misc_feature <222> (1)(558) <223> n = A,T,C or G			
<pre><400> 181 tccytttgkt naggtttkkg agacamccck agacctwaan aatgtttagg cagtgctagt aatttcytcg taatgattct ttattcctct ttcttctgaa gattaatgaa gttgaaaatt ggtagtgtga tagtataagt atctaagtgc agatgaaagt aaattatgca agttagtaat tactcagggt taactaaatt ctactctgtt ccttggctag aaaaaattat aaacaggact attgataata ttctatgttc taaaagttgg gctatacata ttttattccc aggaatatgg kgttcatttt atgaatatta aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa caaaaaaaaa aaaaaaaa</pre>	gttattactt gaggtggata gtgttatata actttaatat ttgttagttt aattattaag cscrggatag	tcctnattct aatacaaaaa tatccattca gctgttgaac gggaagccaa aaatatggaw awgtwtgagt	60 120 180 240 300 360 420 480 540 558
<210> 182 <211> 479 <212> DNA <213> Homo sapien <220> <221> misc_feature			
$\langle 222 \rangle$ (1)(479) $\langle 223 \rangle$ n = A,T,C or G			
<400> 182 acagggwttk grggatgcta agsccccrga rwtygtttga agaggggaaa atggggccta gaagttacag mscatytagy cstcacacag astcccgagt agctgggact acaggcacac ttwgcaattc acgttgccac ctccaactta aacattcttcccac ctaaggttaa actttcccac ccagaaaagg caacttagat	tggtgcgmtgagtcactgaaatatgtgatg	gcacccctgg gcaggccctg tccttagtca	60 120 180 240 300

```
tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant
                                                                         360
  ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara
                                                                         420
  awtgstgara aaattaaaat gttctggtty mactttaaaa araaaaaaaa aaaaaaaaa
                                                                         479
        <210> 183
        <211> 384
        <212> DNA
        <213> Homo sapien
        <400> 183
 aggegggage agaagetaaa geeaaageee aagaagagtg geagtgeeag caetggtgee
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtggtgg cttcagtgct
                                                                          60
                                                                         120
 ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt
 gccagcacca gtggcagctc tggtgcctgt ggtttctcct acaagtgaga ttttagatat
                                                                         180
 tgttaateet gecagtettt etetteaage cagggtgeat eeteagaaae etaeteaaca
                                                                         240
 cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt
                                                                         300
                                                                         360
 gccatttcaa aaaaaaaaaa aaaa
                                                                         384
       <210> 184
       <211> 496
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(496)
       <223> n = A, T, C \text{ or } G
       <400> 184
accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag
                                                                         60
cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga
                                                                        120
aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac
                                                                        180
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact cttcggactg
                                                                        240
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg
                                                                        300
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt
                                                                        360
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst
                                                                        420
                                                                        480
taaaaaaaa aaaaaa
                                                                        496
      <210> 185
      <211> 384
      <212> DNA
      <213> Homo sapien
      <400> 185
gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc
caagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc
                                                                        60
                                                                       120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg
                                                                       180
tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aacttgctca
                                                                       240
ttgccatgtt cagttacaca ttcggcaaag tacagggcaa cagcgatctc tactgggaag
                                                                       300
                                                                       360
gcgcagcgtt accgcctcat ccgg
                                                                       384
      <210> 186
      <211> 577
```

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(577)
      <223> n = A, T, C or G
      <400> 186
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc
                                                                         60
tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt
                                                                        120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc
                                                                        180
teggtgtgaa aggatetece agaaggagtg etegatette eccacacttt tgatgaettt
                                                                        240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac
                                                                        300
cagecetate atgeegttga megtgeegaa gareaeegag eettgtgtgg gggkkqaaqt
                                                                        360
ctcacccaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcqcccaq
                                                                        420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw
                                                                        480
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcatcatcc
                                                                        540
aagatntcgc acagcactna tccagttggg attaaat
                                                                        577
      <210> 187
      <211> 534
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(534)
      \langle 223 \rangle n = A,T,C or G
      <400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw
                                                                         60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact
                                                                        120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta
                                                                        180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat ctttttttt
                                                                        240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc
                                                                        300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttygggagc
                                                                        360
tgatatttga geggaagagt ageettteta etteaceaga cacaacteee ttteatattg
                                                                        420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg
                                                                        480
aggatetece agtttattta ecaettgeae aagaaggegt tttetteete agge
                                                                        534
      <210> 188
      <211> 761
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(761)
      <223> n = A, T, C or G
      <400> 188
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                         60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                        120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                        180
```

```
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                         240
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg
                                                                         300
 ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa
                                                                         360
 acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt
                                                                         420
 gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgtttttt tatnataaaa
                                                                         480
 cttgcccttc attacatgtt tnaaagtggt gtggtgggcc aaaatattga aatgatggaa
                                                                         540
 ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac
                                                                         600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta
                                                                         660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac
                                                                        720
gaaaataata acattgaaga aaaananaaa aaanaaaaaa a
                                                                        761
       <210> 189
       <211> 482
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(482)
       <223> n = A,T,C or G
      <400> 189
tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca
                                                                         60
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca
                                                                        120
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc
                                                                        180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag
                                                                        240
tgataggcac aggccacccg gtacagaccc ctcggctcct gacaggtnga tttcgaccag
                                                                        300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc
                                                                        360
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg
                                                                        420
gttcggccca gctccncgtc caaaaantat tcacccnnct ccnaattgct tgcnggnccc
                                                                        480
CC
                                                                        482
      <210> 190
      <211> 471
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(471)
      \langle 223 \rangle n = A,T,C or G
      <400> 190
tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg
                                                                        60
aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca
                                                                       120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag
                                                                       180
cgcttttgac atacaatgca caaaaaaaa agggggggg gaccacatgg attaaaattt
                                                                       240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt
                                                                       300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtgatcat gantneteta
                                                                       360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaanaa
                                                                       420
tctgtaattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c
                                                                       471
      <210> 191
      <211> 402
      <212> DNA
```

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(402)
      <223> n = A,T,C or G
      <400> 191
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct
                                                                         60
qtcttccact cactqtctqt aagcttttta acccagacwg tatcttcata aatagaacaa
                                                                        120
attetteace agteacatet tetaggacet tittggatte agttagtata agetetteca
                                                                        180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg
                                                                        240
ctcqttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc
                                                                        300
ctttqtqcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc
                                                                        360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca
                                                                        402
      <210> 192
      <211> 601
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(601)
      <223> n = A, T, C \text{ or } G
      <400> 192
                                                                         60
qaqctcqqat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                        120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatcccgyt
                                                                        180
cttttqtqqa aaaactggca cttktctgga actagcarga catcacttac aaattcaccc
                                                                        240
acqaqacact tgaaaggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac
                                                                        300
cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga
                                                                        360
tacatetect gacagtactg aagaacttet tettttgttt caaaageare tettggtgee
                                                                        420
tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac
                                                                        480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag
                                                                        540
cctcqatqta gccggccagc gccaaggcag gcgccgtgag ccccaccagc agcagaagca
                                                                        600
                                                                        601
      <210> 193
      <211> 608
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(608)
      <223> n = A, T, C \text{ or } G
      <400> 193
atacagecca nateceaeca egaagatgeg ettgttgaet gagaaeetga tgeggteaet
                                                                         60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt
                                                                        120
cccaacgcag gcagmagcgg gsccggtcaa tgaactccay tcgtggcttg gggtkgacgg
                                                                        180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac
                                                                        240
ctqcaqcqaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc
                                                                        300
```

```
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcggcctcg
                                                                         360
 gaccagegga caaacggert tgaacageeg caeetcaegg atgeecagtg tgtegegete
                                                                         420
 caggammgsc accagegtgt ccaggtcaat gteggtgaag eceteegegg gtratggegt
                                                                         480
 ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga
                                                                         540
 gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaactc
                                                                         600
 cacgcaat
                                                                         608
       <210> 194
       <211> 392
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(392)
       <223> n = A,T,C or G
       <400> 194
gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc
                                                                          60
                                                                         120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac
                                                                         180
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt
                                                                        240
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg
                                                                        300
                                                                        360
 aaataaatat agttattaaa ggttgtcant cc
                                                                        392
       <210> 195
       <211> 502
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(502)
      <223> n = A, T, C \text{ or } G
      <400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc
                                                                         60
                                                                        120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc
                                                                        180
aagggaaggc cccattccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca
                                                                        240
                                                                        300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact
                                                                        360
gscscacacc cacccagage acgccacccg ccatggggar tgtgctcaag gartcgcngg
gcarcgtgga catcingtcc cagaaggggg cagaatctcc aatagangga cigarcmstt
                                                                        420
                                                                        480
gctnanaaaa aaaaanaaaa aa
                                                                        502
      <210> 196
      <211> 665
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(665)
```

<223> n = A,T,C or G

<400> 196 ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60 cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt 120 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180 actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc 240 300 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360 tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt 420 watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540 600 ttcttaqaat qtataaaggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660 665 aagtg <210> 197 <211> 492 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1) ... (492) <223> n = A, T, C or G<400> 197 60 ttttnttttt tttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg 120 aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag 180 aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa 240 caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac 300 attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct 360 420 tqttcaaaaq tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg 480 492 ancntggctt aa <210> 198 <211> 478 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1) ... (478) <223> n = A, T, C or G<400> 198 tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa 60 tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac 120 tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt 180 tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat 240 300 natatatgtc aatcngattt aagatacaaa acagatccta tggtacatan catcntgtag gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta 360

agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnca

```
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa
                                                                           478
        <210> 199
        <211> 482
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(482)
        \langle 223 \rangle n = A,T,C or G
        <400> 199
 agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
 tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
                                                                           60
 tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                          120
 agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                          180
 tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga
                                                                          240
 aaatttacct ggangaaaag aggetttngg etggggacca teecattgaa eettetetta
                                                                          300
 anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg
                                                                          360
 aacningaen neaccetini ggaatanani ettgaengen teetgaacti geteetetge
                                                                          420
                                                                          480
 ga
                                                                          482
        <210> 200
       <211> 270
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(270)
       <223> n = A, T, C or G
       <400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc
                                                                          60
aaggetgage tgaegeegea gaggtegtgt caegteecae gaeettgaeg eegtegggga
                                                                         120
cagccggaac agagcccggt gaangcggga ggcctcgggg agcccctcgg gaagggcggc
                                                                         180
                                                                         240
ccgagagata cgcaggtgca ggtggccgcc
                                                                         270
       <210> 201
       <211> 419
       <212> DNA
      <213> Homo sapien
       <220>
      <221> misc_feature
      <222> (1)...(419)
      <223> n = A, T, C \text{ or } G
      <400> 201
tttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                         60
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca
                                                                        120
tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg
                                                                        180
                                                                        240
```

```
tctqtqaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag
                                                                       300
tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga
                                                                       360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca
                                                                       419
      <210> 202
      <211> 509
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (509)
      <223> n = A, T, C \text{ or } G
      <400> 202
tttnttttt ttttttt tttttttt tttttttt
                                                                        60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng
                                                                       120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa
                                                                       180
tacncncaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa
                                                                       240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa
                                                                       300
ggaactaaaa taaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta
                                                                       360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng
                                                                       420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca
                                                                       480
                                                                       509
caatggnaat nccnccncnc tggactagt
      <210> 203
      <211> 583
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(583)
      <223> n = A,T,C or G
      <400> 203
ttttttttt tttttttga cccccctctt ataaaaaaca agttaccatt ttattttact
                                                                        60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                       120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                       180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc
                                                                       240
                                                                       300
atttttcttg tctttaaaat tatctaatct ttccattttt tccctattcc aagtcaattt
                                                                       360
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc
                                                                       420
                                                                       480
tacqttaata aaataqcatt ttqtqaagcc agctcaaaag aaggcttaga tccttttatg
                                                                       540
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaaggttt gtgaacattt
attcaaaagc taatataaga tatttcacat actcatcttt ctg
                                                                       583
      <210> 204
      <211> 589
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (589)
```

<223> n = A,T,C or G

```
<400> 204
 tttttttttt tttttttt ttttttnctc ttctttttt ttganaatga ggatcgagtt
 tttcactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca
                                                                          60
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc
                                                                         120
 tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat
                                                                         180
                                                                         240
 tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt
                                                                         300
 attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag
                                                                         360
 cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag
 ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc
                                                                         420
 aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat
                                                                         480
 ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg
                                                                        540
                                                                        589
       <210> 205
       <211> 545
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(545)
       <223> n = A,T,C or G
       <400> 205
tttttntttt tttttcagt aataatcaga acaatattta tttttatatt taaaattcat
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata
                                                                         60
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat
                                                                        120
ttaagatcat agagcttyta agtgaaaaga taaaatttya cctcagaaac tctgagcatt
                                                                        180
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat
                                                                        240
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct
                                                                        300
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt
                                                                        360
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg
                                                                        420
aaggattaga tatgtttcct ttgccaatat taaaaaaata ataatgttta ctactagtga
                                                                        480
                                                                        540
aaccc
                                                                       545
      <210> 206
      <211> 487
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(487)
      <223> n = A,T,C or G
      <400> 206
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna
                                                                        60
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt
                                                                       120
cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac
                                                                       180
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag
                                                                       240
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt
                                                                       300
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag
                                                                       360
aactettega acegetteet caaaggenge tgecacattt gtggentetn ttgeacttgt
                                                                       420
                                                                       480
```

ttcaaaa

```
<210> 207
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(332)
      \langle 223 \rangle n = A,T,C or G
      <400> 207
                                                                         60
tqaattqqct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact
                                                                        120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana
                                                                        180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca
                                                                        240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg
                                                                        300
                                                                        332
aaaagaaggc agcctaggcc ctggggagcc ca
      <210> 208
      <211> 524
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(524)
      <223> n = A, T, C \text{ or } G
      <400> 208
agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg
                                                                         60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat
                                                                        120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac
                                                                        180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact
                                                                        240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa
                                                                        300
qtaaataqaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc
                                                                        360
atgageceag acaetgaeat caaactaage ceaettagae teeteaceae cagtetgtee
                                                                         420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa
                                                                        480
                                                                         524
aaaccattac ctgatccact tccggtaatg caccaccttg gtga
      <210> 209
      <211> 159
      <212> DNA
      <213> Homo sapien
      <400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg
                                                                         60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca
                                                                         120
caaaggacto togacocaaa otgooccaga coctotoca
                                                                         159
      <210> 210
      <211> 256
      <212> DNA
      <213> Homo sapien
```

```
<220>
        <221> misc_feature
        <222> (1)...(256)
        <223> n = A, T, C \text{ or } G
        <400> 210
 actecetgge agacaaagge agaggagaga getetgttag ttetgtgttg ttgaactgee
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta
                                                                          60
                                                                         120
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat
 ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca
                                                                         180
                                                                         240
 ccaggatgct aaatca
                                                                         256
       <210> 211
       <211> 264
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(264)
       <223> n = A,T,C or G
       <400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg
                                                                         60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga
                                                                        120
ggggagatac attengaaag aggaetgaaa gaaataetea agtnggaaaa cagaaaaaga
                                                                        180
                                                                        240
aaaaaaggag caaatgagaa gcct
                                                                        264
      <210> 212
      <211> 328
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(328)
      <223> n = A,T,C or G
      <400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa
ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagecggcag
                                                                         60
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag
                                                                        120
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta
                                                                        180
cccctacnac tctttactct ctgganaggg ccagtggtgg tagctataag cttggccaca
                                                                        240
                                                                        300
ttttttttc ctttattcct ttgtcaga
                                                                       328
      <210> 213
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
```

```
<222> (1)...(250)
      <223> n = A,T,C or G
      <400> 213
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt
                                                                        60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                       120
                                                                       180
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct
                                                                       240
tctcatcggt
                                                                       250
      <210> 214
      <211> 444
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(444)
      <223> n = A,T,C or G
      <400> 214
                                                                        60
acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag
gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg
                                                                       120
tttatatatq caqcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt
                                                                       180
tqaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac
                                                                       240
ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat
                                                                       300
tttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag
                                                                       360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt
                                                                       420
                                                                        444
actttgctct ccctaatata cctc
      <210> 215
      <211> 366
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(366)
      <223> n = A,T,C or G
      <400> 215
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt
                                                                         60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                        120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
                                                                        180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacct
                                                                        240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa
                                                                        300
tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt
                                                                        360
                                                                        366
ggtgcc
      <210> 216
      <211> 260
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc_feature
        <222> (1)...(260)
        <223> n = A,T,C or G
        <400> 216
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat
                                                                          60
                                                                         120
 taataaaaag tnnaaaaggc ctcttctcaa ctttttccc ttnggctgga aaatttaaaa
 atcaaaaatt teetnaagtt nteaagetat eatatatet ntateetgaa aaageaacat
                                                                         180
                                                                         240
 aattcttcct tccctccttt
                                                                        260
       <210> 217
       <211> 262
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(262)
       <223> n = A,T,C or G
       <400> 217
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta
                                                                         60
 tcttgcctat aattttctat tttaataagg aaatagcaaa ttggggtggg gggaatgtag
 ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt
                                                                        120
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta
                                                                        180
                                                                        240
 atateettea tgettgtaaa gt
                                                                        262
       <210> 218
       <211> 205
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(205)
      <223> n = A,T,C or G
      <400> 218
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc
                                                                        60
aggeeteece agttetactg acetttgtee ttangtntna ngteeagggt tgetaggaaa
                                                                       120
                                                                       180
anaaatcagc agacacaggt gtaaa
                                                                       205
      <210> 219
      <211> 114
      <212> DNA
      <213> Homo sapien
      <400> 219
tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg gccccatcca
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga
                                                                        60
                                                                       114
      <210> 220
      <211> 93
```

```
<212> DNA
      <213> Homo sapien
      <400> 220
actagecage acaaaaggea gggtageetg aattgettte tgetetttae atttettta
                                                                         60
aaataaqcat ttagtgctca gtccctactg agt
                                                                         93
      <210> 221
      <211> 167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (167)
      <223> n = A, T, C \text{ or } G
      <400> 221
actangtgca ggtgcgcaca aatatttgtc gatattccct tcatcttgga ttccatgagg
                                                                         60
tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc
                                                                        120
ccccactac cttccctgac gctccccana aatcacccaa cctctgt
                                                                        167
      <210> 222
      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 222
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc
                                                                         60
gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa
                                                                        120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa
                                                                        180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt
                                                                        240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt
                                                                        300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t
                                                                        351
      <210> 223
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A,T,C or G
      <400> 223
                                                                         60
aaaacaaaca aacaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat
tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga
                                                                        120
ttaaaatgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc
                                                                        180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc
                                                                        240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttggtggg ggaaanagtt
                                                                        300
ataggaccac agtottcact totgatactt gtaaattaat ottttattgc acttgttttg
                                                                        360
                                                                        383
accattaagc tatatgttta aaa
```

<210> 224

```
<211> 320
       <212> DNA
       <213> Homo sapien
       <400> 224
 cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga
 aaaagtttgt gacattgtag tagggagtgt gtacccctta ctccccatca aaaaaaaat
                                                                       60
 ggatacatgg ttaaaggata raagggcaat attttatcat atgttctaaa agagaaggaa
                                                                      120
 gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac
                                                                      180
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcagt
                                                                      240
                                                                      300
 tttaractcm gcattgtgac
                                                                      320
       <210> 225
       <211> 1214
       <212> DNA
       <213> Homo sapien
       <400> 225
gaggactgca gcccgcactc gcagccctgg caggcggcac tggtcatgga aaacgaattg
ttctgctcgg gcgtcctggt gcatccgcag tgggtgctgt cagccgcaca ctgtttccag
                                                                      60
aacteetaca ecateggget gggeetgeae agtettgagg eegaceaaga geeagggage
                                                                     120
cagatggtgg aggccagcct ctccgtacgg cacccagagt acaacagacc cttgctcgct
                                                                     180
aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc
                                                                     240
atcagcattg cttcgcagtg ccctaccgcg gggaactctt gcctcgtttc tggctggggt
                                                                     300
                                                                     360
ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct
                                                                     420
gaggaggtet geagtaaget etatgaeeeg etgtaeeaee eeageatgtt etgegeegge
ggagggcaag accagaagga ctcctgcaac ggtgactctg gggggcccct gatctgcaac
                                                                     480
gggtacttgc agggccttgt gtctttcgga aaagccccgt gtggccaagt tggcgtgcca
                                                                     540
ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt
                                                                     600
taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaaggaatt
                                                                     660
caggaatate tgtteecage cecteeteec teaggeecag gagteeagge ceceageece
                                                                     720
tecteectea aaccaagggt acagateece ageceeteet eecteagace caggagteea
                                                                     780
gacccccag ccctcctcc ctcagaccca ggagtccagc ccctcctccc tcagacccag
                                                                     840
gagtccagac ccccagccc ctcctccctc agacccaggg gtccaggccc ccaacccctc
                                                                     900
ctccctcaga ctcagaggtc caagccccca acccctcctt ccccagaccc agaggtccag
                                                                     960
                                                                    1020
gtcccagccc ctcctccctc agacccagcg gtccaatgcc acctagactc tccctgtaca
cagtgcccc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc
                                                                    1080
                                                                    1140
1200
aaaaaaaaa aaaa
                                                                    1214
      <210> 226
      <211> 119
      <212> DNA
      <213> Homo sapien
      <400> 226
acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa
agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt
                                                                     60
                                                                    119
     <210> 227
     <211> 818
     <212> DNA
     <213> Homo sapien
     <400> 227
```

tttttgctac acggacggtt aattttcctc gagaaagcca gcttgtcccc agggcctcct ggaaagggtg acctgctggc gccatccact gacaggctct aaagccattc caagaggata	gggacgacca atatggggtc cttagcacaa ctctggagga cgctcggcct ttccaatcag caggagcagt caccctcagc tgtcttggga ggacatgaag gcctcaagc ccacaaatcc tgaggactgt aggttttcag	ccttttcatt tttgtgaaat aaggtggtga tctctgaacc ccacttctga ccaagagttt agagaagccg tgcgccagc ctgaggacac cggctgaggg agaccatacc ctcagcctgg	ctttgcaaaa ctgtgtaraa ttgacaggca aggatggaac gaaccccat tcaaagataa agagcttaac ctttgagagg tgggcttcaa cagcaaccac atgaagcaac ctttgggctg	acactgggtt ccgggctttg gggagacagt ggcagacccc ctaacttcct cgtgacaact tctggtcgtt ccactacccc cactgagttg tctcctcccc gagacccaaa	ttctgagaac caggggagat gacaaggcta tgaaaacgaa actggaaaag accatctaga tccagagaca atgaacttct tcatgagagg tttctcacgc cagtttggct	60 120 180 240 300 360 420 480 540 600 660 720 780 818
	> 228 > 744					
	> DNA > Homo sapie	en				
	> 228					
actggagaca	> 228 ctgttgaact ttgacatacc					60 120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
	acattggggt					300
	aggccagttt					360
	gaatggcttg					420 480
	ggatgcttgt					540
	ttggccactc ccttggccca					600
	taatgttcct					660
	tggaccagag					720
	aagtagctgg					744
<211	> 229 > 300					
	> DNA > Homo sapi	en				
	> 229					
cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
	ttgtttttta					180 240
ttgtatgtga	cagccaactc ctccttgccc	tgagaaggtc	gtgtgggga	accigcagag	ccactgacat	300
Cactaggete	Ciccingue		geeeegeea	9090999090	ccaccgacac	300
	> 230					
	> 301					
	<pre>> DNA > Homo sapi</pre>	en				
<400	> 230					
	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120

caatataaag teetggttea eacteaggaa egagagetga eeeagttaag ggagaagttg egggaaggga gagatgeete eeteteattg aatgageate teeaggeeet eeteaeteeg gatgaacegg acaagteeea ggggeaggae eteeaagaaa eagaeetegg eegegaeeae g	180 240 300 301
<210> 231 <211> 301 <212> DNA <213> Homo sapien	
<400> 231	
gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcattttagc caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc c	60 120 180 240 300 301
<210> 232	
<211> 301 <212> DNA	
<213> Homo sapien	
<400> 232	
agtaggtatt tegtgagaag tteaacacca aaactggaac atagttetee tteaagtgtt	60
3303404303 33900000019 delected ataachtent chanathand accommen	120
agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca cgtgctgtac caagtgctgg tgccagcctg ttacctgttc tcactgaaaa tctggctaat	180
gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact	240
g g	300
	301
<210> 233 <211> 301	
<211> 301 <212> DNA	
<213> Homo sapien	
•	
<400> 233	
atgactgact teceagtaag getetetaag gggtaagtag gaggateeac aggatttgag	60
m-3-1-1-330 cookgagacc gullyaluca accororrat tetoagagaga gasa-	120
cctagaagtt acagagcatc tagctggtgc gctggcaccc ctggcctcac acagactccc gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg	180
tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa	240
C genagagada atectateaa	300
	301
<210> 234 <211> 301	
<212> DNA	
<213> Homo sapien	
<400> 234	
aggtectaca categagaet catecatgat tgatatgaat ttaaaaatta caagcaaaga	60
- Jacobs accardated reference to the contract of the contract	120
tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct cgcctcatga cagcaagttc aatgttttg ccacctgact gaaccacttc caggagtgcc	180
ttgatcacca gcttaatggt cagatcatct gcttcaatgg cttcgtcagt atagttcttc	240
5 Cologicage acagetette	300

```
301
t
      <210> 235
      <211> 283
      <212> DNA
      <213> Homo sapien
      <400> 235
tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg
                                                                        60
aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg
                                                                       120
tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata
                                                                       180
atgttatctt tgaactgatg ctcataggag agaatataag aactctgagt gatatcaaca
                                                                       240
                                                                       283
ttagggattc aaagaaatat tagatttaag ctcacactgg tca
      <210> 236
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 236
aggtecteca ceaactgeet gaageaeggt taaaattggg aagaagtata gtgeageata
                                                                        60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg
                                                                       120
teggageage ateattaata eeaageagaa tgegtaatag ataaataeaa tggtatatag
                                                                       180
tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta
                                                                       240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc
                                                                       300
                                                                       301
      <210> 237
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 237
                                                                        60
caqtqqtaqt qqtqqtqqac gtggcgttgg tcgtggtgcc ttttttggtg cccgtcacaa
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg
                                                                       120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct
                                                                       180
ttqqqtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta
                                                                       240
gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcctttatc
                                                                       300
                                                                       301
t
      <210> 238
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 238
gggcaggttt ttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt
                                                                        60
                                                                       120
gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca
ccttgagact tccggagtcg aggctctcca gggttcccca gcccatcaat cattttctgc
                                                                       180
acccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca
                                                                       240
gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta
                                                                       300
                                                                       301
      <210> 239
      <211> 239
```

86

<212> DNA <213> Homo sapien <400> 239 ataagcagct agggaattct ttatttagta atgtcctaac ataaaagttc acataactgc ttctgtcaaa ccatgatact gagctttgtg acaacccaga aataactaag agaaggcaaa cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac 120 attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga 180 239 <210> 240 <211> 300 <212> DNA <213> Homo sapien <400> 240 ggtcctaatg aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt gggatctgcc ctccagtgga accttttaag gaagaagtgg gcccaagcta agttccacat 60 gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg 120 ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac 180 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 240 300 <210> 241 <211> 301 <212> DNA <213> Homo sapien <400> 241 gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga cctctttgga ggaaactcca gcagctatgt tggtgtctct gagggaatgc aacaaggctg 60 ctcctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag 120 tgtgaagaac cagcctgagg tgacagaac ggaagcaaac aggaacagcc agtcttttct 180 tectectect gteataeggt eteteteaag cateetttgt tgteagggge etaaaaggga 240 300 301 <210> 242 <211> 301 <212> DNA <213> Homo sapien <400> 242 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 60 gtcttcaaga atatatcatt cctttttcac tagaacccat tcaaaatata agtcaagaat 120 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 180 taagtaccca aagttttata aatcaaaagc cctaatgata accattttta gaattcaatc 240 300 301 <210> 243 <211> 301 <212> DNA <213> Homo sapien <400> 243 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 60 120

tgacgtgcag tcggactctg tggcccaagg gtatggct gctggtttgt ccagatggca agacagtaga agcagagg tcactaccgc atgttccaga aaggacagga gacgtcca t	ct gcccacggga ctgtaacccg 240
<210> 244 <211> 300 <212> DNA <213> Homo sapien	
<400> 244	
gctggtttgc aagaatgaaa tgaatgattc tacagcta	gg acttaacctt gaaatggaaa 60
gtcatgcaat cccatttgca ggatctgtct gtgcacat	
ccagggacct tggaaacagt tgacactgta aggtgcttagggtgttgta atggtgaaaa cgtcttcctt ctttattg	
actgtttgtc ttttgtgtat cttttttaaa ctgtaaag	
<210> 245 <211> 301 <212> DNA	
<213> Homo sapien	
<400> 245	
gtctgagtat ttaaaatgtt attgaaatta tccccaac	
tatatactta gataaaaaat gaggtgaatt actatcca	
aaggccagga gatattgtca ttaatgtara cttcagga gttttcaaag agcagagatg caattaaata ttgtttag	
agctaataaa atgaaagacc taatttctaa agcaattc	
<210> 246	
<211> 301 <212> DNA	
<213> Homo sapien	
<400> 246	
ggtctgtcct acaatgcctg cttcttgaaa gaagtcgg	ca ctttctagaa tagctaaata 60
acctgggctt attttaaaga actatttgta gctcagatt	
agtgcttctt gtgaaaatta aataaaacag ttaattca	
caaatgtgtc ttacaaaca cgttcctaac aaggtatg	
С	301
<210> 247	
<211> 301 <212> DNA	
<213> Homo sapien	
<400> 247	
aggtcctttg gcagggctca tggatcagag ctcaaactg	gg agggaaaggc atttcgggta 60
gcctaagagg gcgactggcg gcagcacaac caaggaagg	
gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaccttgatgat caaggttggg gcttaagtgg attaaggga	
cttttcaaac catgaagtca ggctctgtat ccctccttt	
a	301

```
<210> 248
        <211> 301
        <212> DNA
        <213> Homo sapien
        <400> 248
 aggteettgg agatgeeatt teageegaag gaetettetw tteggaagta caeeeteaet
                                                                          60
 attaggaaga ttcttagggg taattttct gaggaaggag aactagccaa cttaagaatt
                                                                         120
 acaggaagaa agtggtttgg aagacagcca aagaaataaa agcagattaa attgtatcag
                                                                         180
 gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag
 ctaatgagac tggatttttg ftttttatgt tgtgtgtcgc agagctaaaa actcagttcc
                                                                        240
                                                                        300
                                                                        301
       <210> 249
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 249
 gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag
 ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc
                                                                         60
 ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc
                                                                        120
                                                                        180
 catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag
 actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt
                                                                        240
                                                                        300
                                                                        301
       <210> 250
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 250
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc
                                                                        60
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac
                                                                        120
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta
                                                                       180
                                                                       240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc
                                                                       300
а
                                                                       301
      <210> 251
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 251
gccgaggtcc tacatttggc ccagtttccc cctgcatcct ctccagggcc cctgcctcat
                                                                        60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat
                                                                       120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct
                                                                       180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccggaa
                                                                       240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct
                                                                       300
                                                                       301
      <210> 252
      <211> 301
```

```
<212> DNA
      <213> Homo sapien
      <400> 252
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca
                                                                        60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata
                                                                       120
tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa
                                                                       180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt
                                                                       240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc
                                                                       300
                                                                       301
      <210> 253
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 253
ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc
                                                                        60
caactaaaaa aaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct
                                                                       120
tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg
                                                                       180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt
                                                                       240
tccatagtgc ccacagggta ttcctcacat tttctccata ggaaaatgct ttttcccaag
                                                                       300
                                                                       301
      <210> 254
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 254
cgctgcgcct ttcccttggg ggagggcaa ggccagaggg ggtccaagtg cagcacgagg
                                                                        60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc
                                                                       120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa
                                                                       180
gaaaaaaata aagctttgga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc
                                                                       240
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc
                                                                       300
                                                                       301
      <210> 255
      <211> 302
      <212> DNA
      <213> Homo sapien
      <400> 255
agcttttttt ttttttttt ttttttttt ttcattaaaa aatagtgctc tttattataa
                                                                       60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat
                                                                       120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg
                                                                       180
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta
                                                                       240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac
                                                                      300
aa
                                                                       302
      <210> 256
      <211> 301
      <212> DNA
      <213> Homo sapien
```

```
<220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 256
 gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct
                                                                          60
 aggaccetee tecceacace teaatecace aaaceateca taatgeacee agataggeee
                                                                         120
 acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat
                                                                         180
 aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt
                                                                         240
 gtggcctctc ggcctggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt
                                                                         300
 t
                                                                         301
       <210> 257
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 257
gttgtggagg aactctggct tgctcattaa gtcctactga ttttcactat cccctgaatt
                                                                         60
tececaetta tttttgtett teaetatege aggeettaga agaggtetae etgeeteeag
                                                                        120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat
gtcacattac tecetteagt gatttettgt agaagtgeea atecetgaat gecaceaaga
                                                                        180
                                                                        240
tottaatott cacatottta atottatoto titigactoot otttacacog gagaaggoto
                                                                        300
                                                                        301
      <210> 258
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C or G
      <400> 258
cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc
                                                                        60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc
                                                                       120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg
                                                                       180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat
                                                                       240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac
                                                                       300
t
                                                                       301
      <210> 259
      <211> 301
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(301)
     <223> n = A,T,C or G
     <400> 259
```

```
tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttqqq
                                                                         60
gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa
                                                                        120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaqqtctqt
                                                                        180
tecageteae ateteatetg catgeageae ggaceggatg egeceaetgg gtettggett
                                                                        240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg
                                                                        300
                                                                        301
      <210> 260
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 260
ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaaat aagcaatggt
                                                                        60
aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa
                                                                        120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac
                                                                        180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc
                                                                       240
actgagacat cagtacetge cegggeggee getegageeg aattetgeag atatecatea
                                                                       300
                                                                        301
      <210> 261
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 261
aaatattcga gcaaatcctg taactaatgt gtctccataa aaggctttga actcagtgaa
                                                                        60
totgottoca tocacgatto tagoaatgac ototoggaca toaaagotoc tottaaqqtt
                                                                       120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aaggttcaat
                                                                       180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag
                                                                       240
ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc
                                                                       300
                                                                       301
      <210> 262
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 262
gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc
                                                                        60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc
                                                                       120
cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga
                                                                       180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgccc
                                                                       240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat
                                                                       300
                                                                       301
      <210> 263
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C or G
```

<400> 263 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 120 taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 180 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 240 g 300 301 <210> 264 <211> 301 <212> DNA <213> Homo sapien <400> 264 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 60 gtggatagat ctagaattgt aacattttaa gaaaaccata scatttgaca gatgagaaag 120 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 180 accetteata taaatteact atettggett gaggeactee ataaaatgta teaegtgeat 240 300 301 <210> 265 <211> 301 <212> DNA <213> Homo sapien <400> 265 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 60 catattettg gaagteteta atcaactttt gtteeatttg ttteatttet teaggaggga 120 ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag 180 cagtecaagg ctttgacatg teaacaacea geataactag agtateette agagataegg 240 300 301 <210> 266 <211> 301 <212> DNA <213> Homo sapien <400> 266 taccgtctgc ccttcctccc atccaggcca tctgcgaatc tacatgggtc ctcctattcg acaccagate actetteet etacceacag gettgetatg ageaagagae acaaceteet 60 ctcttctgtg ttccagcttc ttttcctgtt cttcccaccc cttaagttct attcctgggg 120 atagagacac caatacccat aacctetete etaageetee ttataaccca gggtgcacag 180 cacagactee tgacaactgg taaggeeaat gaactgggag etcacagetg getgtgeetg 240 300 301 <210> 267 <211> 301 <212> DNA <213> Homo sapien <400> 267 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60

```
gttctcaqtq ctgagtccat ccaggaaaag ctcacctaga ccttctgagg ctgaatcttc
                                                                        120
atcctcacaq qcaqcttctg agagcctgat attcctagcc ttgatggtct ggagtaaagc
                                                                        180
ctcattctga ttcctctct tcttttcttt caagttggct ttcctcacat ccctctgttc
                                                                        240
aattegette agettgtetg etttageeet cattteeaga agettettet etttggeate
                                                                        300
                                                                        301
t.
      <210> 268
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 268
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta
                                                                        60
gatcttggga gagctggttc ttctaaggag aaggaggaag gacagatgta actttggatc
                                                                        120
tcgaagagga agtctaatgg aagtaattag tcaacggtcc ttgtttagac tcttggaata
                                                                        180
tqctqqqtqq ctcaqtqagc ccttttggag aaagcaagta ttattcttaa ggagtaacca
                                                                        240
cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact
                                                                        300
                                                                        301
а
      <210> 269
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 269
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat
                                                                        60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact
                                                                        120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta
                                                                        180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta
                                                                        240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc
                                                                        300
                                                                        301
      <210> 270
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgctt ataaaattaa ttaagcctta
                                                                        60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga
                                                                       120
gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa
                                                                        180
                                                                       240
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa
                                                                        300
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac
                                                                        301
a
      <210> 271
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A,T,C \text{ or } G
```

```
<400> 271
  aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt
  tttatagctc atctttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca
                                                                            60
  gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggtccaagg
                                                                           120
  tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt
                                                                           180
  tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca
                                                                           240
                                                                           300
                                                                           301
        <210> 272
        <211> 301
        <212> DNA
        <213> Homo sapien
        <400> 272
  taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc
  ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga
                                                                           60
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcatccaca
                                                                          120
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc
                                                                          180
 ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag
                                                                          240
                                                                          300
 g
                                                                          301
        <210> 273
        <211> 301
        <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       \langle 223 \rangle n = A,T,C or G
       <400> 273
 acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt attttttgg
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa
                                                                          60
 gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc
                                                                         120
 ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt
                                                                         180
gggactinty titacngagm accetgeeeg sgegeeeteg makenganti eegesanane
                                                                         240
                                                                         300
                                                                         301
       <210> 274
       <211> 301
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      \langle 223 \rangle n = A,T,C or G
      <400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa
                                                                         60
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca
                                                                        120
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc
                                                                        180
aattgtgctt cttttgataa gaagetttet tggtcatate aggaaattee aganaaagte
                                                                        240
                                                                        300
```

```
C
                                                                         301
      <210> 275
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C \text{ or } G
      <400> 275
teggtgteag cageacgtgg cattgaacat tgcaatgtgg ageccaaace acagaaaatg
                                                                          60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc
                                                                        120
tggccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag
                                                                        180
tcaaqaqact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc
                                                                        240
agatatecat cacactggeg gnegetegan catgeateta gaaggneeaa ttegeeetat
                                                                        300
                                                                        301
      <210> 276
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 276
tqtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat
                                                                         60
ttatcatqtq acttctaatt agaaaatqta tccaaaagca aaacagcaga tatacaaaat
                                                                        120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc
                                                                        180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt
                                                                        240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat
                                                                        300
                                                                        301
      <210> 277
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(301)
      <223> n = A, T, C \text{ or } G
      <400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag
                                                                         60
                                                                        120
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg
gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccca ccctcgtcct
                                                                        180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga
                                                                        240
gttcnctgtc gattacatct gaccagtctc ctttttccga agtccntccg ttcaatcttg
                                                                        300
                                                                        301
С
      <210> 278
      <211> 301
      <212> DNA
      <213> Homo sapien
```

```
<220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G
        <400> 278
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca
                                                                          60
                                                                         120
 cagtetetae tgttattatg cattacetgg gaatttatat aageeettaa taataatgee
                                                                         180
 aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaggttt
                                                                         240
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt
                                                                         300
 С
                                                                         301
       <210> 279
       <211> 301
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 279
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact
                                                                         60
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc
                                                                        120
 ttagaccttt accttccagc caccccacag tgcttgatat ttcagagtca gtcattggtt
                                                                        180
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac
                                                                        240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag
                                                                        300
                                                                        301
       <210> 280
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 280
ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg
                                                                         60
tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct
                                                                        120
tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg
                                                                        180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag
                                                                        240
                                                                       300
                                                                       301
      <210> 281
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 281
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc
gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca
                                                                        60
                                                                       120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa
                                                                       180
tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc
                                                                       240
```

tgacaagtga aacaggatct tacgatggag ttttgta g	tga aaacaaagtt gcagtacctc 300 301
<210> 282 <211> 301 <212> DNA <213> Homo sapien	
<400> 282	
caggtactac agaattaaaa tactgacaag caagtag	
tccagaaccc aaaaattaag aaattcaaaa agacatt agcgcagaag caaagcccag gcagaaccat gctaacc	
cgcagaagca aagcccaggc agaaccatgc taacctt	
cagaagcaaa gcccaggcag aacatgctaa ccttaca	
a	301
<210> 283	
<211> 301	
<212> DNA <213> Homo sapien	
(2137 Homo Supre.)	
<400> 283	
atctgtatac ggcagacaaa ctttatarag tgtagag cactttgagg gctttataat aatatgctgc ttgaaaa	
gtgcatctcc agacatagta aggggttgct ctgacca	
acttcccagg ttttatgcaa aaattttgtt aaattct	ata atggtgatat gcatctttta 240
ggaaacatat acatttttaa aaatctattt tatgtaa	gaa ctgacagacg aatttgcttt 300 301
g	301
<210> 284	
<211> 301 <212> DNA	
<213> Homo sapien	
<400> 284 caggtacaaa acgctattaa gtggcttaga atttgaa	cat trgtggtctt tatttacttt 60
gcttcgtgtg tgggcaaagc aacatcttcc ctaaata	
gcagattagg tttttgacaa aacaaacagg ccaaaac	ggg gctgacctgg agcagagcat 180
ggtgagaggc aaggcatgag agggcaagtt tgttgtg	gac agatotgtgo otactttatt 240 gga tatatacagt ottagaaatt 300
actggagtaa aagaaaacaa agttcattga tgtcgaa	301
_	
<210> 285	
<211> 301 <212> DNA	
<213> Homo sapien	
.220	
<220> <221> misc feature	
<222> (1)(301)	
<223> n = A,T,C or G	
<400> 285	
acatcaccat gatcggatcc cccacccatt atacgtt	
aargatcatt agtgttttaa aaaaaatact gaaaact	cct tctgcatccc aatctctaac 120

WO 00/04149

caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg attaaatatg tctgacttct tttgaggtca cacgactagg caaatgctat ttacgatctg caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag t	180 240 300 301
<210> 286 <211> 301 <212> DNA <213> Homo sapien	501
<400> 286	
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct	60
by database tricyclica cadiquatca fictagrada aaadgacagt somethis	120
accordingly geological taddadator farafficter totalties.	180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg	240
t and the same same same same same same same sam	300 301
<210> 287	301
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 287	
tacagatetg ggaactaaat attaaaaatg agtgtggerg gatatatgga garatata	
	60 120
anadyacteg getatgaaty catadtttag geagraggge caraatgate seems	180
ccgtggttat ctcctccca gcttggctgc ctcatgttat cacagtattc cattttgttt gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc	240
t state of the sta	300 301
<210> 288	201
<211> 301	
<212> DNA	
<213> Homo sapien	
<400> 288	
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag	60
	60 120
saccition adda diff correspond to the saccionation	180
adaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa	240
a gradutedat dattagada gttadadada	300 301
<210> 289	301
<211> 301	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)(301)	
<223> n = A,T,C or G	
<400> 289	

ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgctcc tgg gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atc ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cct cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aag tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aac a	eatctttg 120 gacttaa 180 gagaaaga 240
<210> 290 <211> 301 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(301) <223> n = A,T,C or G	
<pre><400> 290 acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tct tgactgatct gttcatttct ctcacagctc ttacccccaa aagcttttcc acc ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aat gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg cta tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taa a</pre>	ctaagtg 120 gaacatg 180 gcagtgc 240
<210> 291 <211> 301 <212> DNA <213> Homo sapien	
<pre><400> 291 caggtaccaa tttcttctat cctagaaaca tttcatttta tgttgttgaa aca tatatcagct agatttttt tctatgcttt acctgctatg gaaaatttga cac tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gta agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaa acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgt. a</pre>	attctgc 120 gttcaat 180 ggcctaa 240
<210> 292 <211> 301 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(301) <223> n = A,T,C or G	
<400> 292 accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tcctgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttaaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctattaacacaa cacagacccc acagtcctat atgccacaaa cacatttcca taaaa	ggtattc 120 cnagatg 180 cacactc 240

```
<210> 293
         <211> 301
        <212> DNA
        <213> Homo sapien
        <400> 293
  ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc
  ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt
                                                                          60
  aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt
                                                                         120
  gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg
                                                                         180
  ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat
                                                                         240
                                                                         300
  g
                                                                         301
        <210> 294
        <211> 301
        <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(301)
       <223> n = A,T,C or G
       <400> 294
 tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag
 attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag
                                                                         60
 tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag
                                                                        120
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc
                                                                        180
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt
                                                                        240
                                                                        300
                                                                        301
       <210> 295
       <211> 305
       <212> DNA
       <213> Homo sapien
       <400> 295
gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaa gtgtctttgt ttaaaattac
                                                                         60
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                        120
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                        180
totcagaaco atttoacoca gacagootgt ttotatootg tttaataaat tagtttgggt
                                                                       240
                                                                       300
tctct
                                                                       305
      <210> 296
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 296
aggractatg ggaagctgct aaaaraatat ttgatagtaa aagtatgtaa tgtgctatct
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg
                                                                        60
attaaataga attaataaac caatargagg aaacatgaaa ccatgcaatc tactatcaac
                                                                       120
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt
                                                                       180
                                                                       240
```

```
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg
                                                                         300
C
                                                                         301
      <210> 297
      <211> 300
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(300)
      \langle 223 \rangle n = A,T,C or G
      <400> 297
actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta
                                                                         60
aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtctagaga
                                                                        120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt
                                                                        180
tecateattg ggagtgeact ggeeatecet caaaatttgt etgggetgge etgagtggte
                                                                        240
accgcacctc ggccgcgacc acgctaagcc gaattetgca gatatecate acactggcgg
                                                                        300
      <210> 298
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C or G
      <400> 298
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg
                                                                         60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg
                                                                        120
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct
                                                                        180
gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttccccta
                                                                        240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg
                                                                        300
                                                                        301
      <210> 299
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 299
gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggtctctgc
                                                                         60
tcactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc
                                                                        120
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg
                                                                        180
gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct
                                                                        240
cggcctccca aagtgctgga attataggca tgagtcaaca cgcccagcct aaagatattt
                                                                        300
                                                                        301
      <210> 300
      <211> 301
      <212> DNA
      <213> Homo sapien
```

```
<400> 300
  attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga
  tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca
                                                                          60
  gctgcattcc acaaggttct cagcctaatg agtttcacta cctgccagtc tcaaaactta
                                                                         120
  gtaaagcaag accatgacat tcccccacgg aaatcagagt ttgccccacc gtcttgttac
                                                                         180
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat
                                                                         240
                                                                         300
                                                                         301
        <210> 301
        <211> 301
        <212> DNA
        <213> Homo sapien
        <400> 301
 ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt
                                                                          60
 gggaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaaagacc
                                                                         120
 ctcagagctg agacacccac aacagtggga gctcacaaag accctcagag ctgagacacc
                                                                         180
                                                                        240
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt
                                                                        300
                                                                        301
       <210> 302
       <211> 301
       <212> DNA
       <213> Homo sapien
       <400> 302
aggtacacat ttagcttgtg gtaaatgact cacaaaactg attttaaaat caagttaatg
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac
                                                                         60
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg
                                                                        120
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca
                                                                        180
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg
                                                                        240
                                                                        300
                                                                        301
       <210> 303
       <211> 301
       <212> DNA
       <213> Homo sapien
      <400> 303
aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt
                                                                        60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac
tggctaatgg aactaccgct tgcatgttaa aaatggtggt ttgtgaaatg atcataggcc
                                                                       120
agtaacgggt atgttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc
                                                                       180
                                                                       240
categatttt atatetgggg tetagaaaag gagttaatet gtttteeete ataaatteae
                                                                       300
                                                                       301
      <210> 304
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 304
acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaat
                                                                        60
```

```
tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc
                                                                        120
ctttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtqcaqt
                                                                        180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactqa
                                                                        240
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct
                                                                        300
                                                                        301
      <210> 305
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      \langle 223 \rangle n = A,T,C or G
      <400> 305
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag
                                                                         60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatqqqcq
                                                                        120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatqcctaq
                                                                        180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa
                                                                        240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag
                                                                        300
                                                                        301
      <210> 306
      <211> 8
      <212> PRT
      <213> Homo sapien
      <400> 306
Val Leu Gly Trp Val Ala Glu Leu
      <210> 307
      <211> 637
      <212> DNA
      <213> Homo sapien
      <400> 307
acagggratg aagggaaagg gagaggatga ggaagccccc ctgggggattt ggtttggtcc
                                                                        60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac
                                                                        120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt
                                                                        180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca
                                                                       240
cacatagcac eggagatatg agateaacag tttettagee atagagatte acageecaga
                                                                       300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgq qattqqtqtq
                                                                       360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga
                                                                       420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aqqtaqtqaa
                                                                       480
acticating ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca
                                                                       540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg
                                                                       600
ttacagatac tggggcagca aataaaactg aatcttg
                                                                       637
      <210> 308
      <211> 647
      <212> DNA
      <213> Homo sapien
```

<220> <221> misc_feature <222> (1)...(647) <223> n = A,T,C or G<400> 308 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa 60 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 120 ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg 180 ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt 240 cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct 300 cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 360 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 420 tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 480 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 540 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 600 647 <210> 309 <211> 460 <212> DNA <213> Homo sapien <400> 309 actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 60 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 120 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg 180 ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctacccag 240 ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 300 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 360 ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt 420 460 <210> 310 <211> 539 <212> DNA <213> Homo sapien <400> 310 acgggactta tcaaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 60 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 120 gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa 180 taatetttat ggeagagaaa getaaaatee tttagettge gtgaatgate aettgetgaa 240 ttcctcaagg taggcatgat gaaggaggt ttagaggaga cacagacaca atgaactgac 300 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac 360 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 420 atattttcac ccccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 480 539 <210> 311 <211> 526 <212> DNA

<213> Homo sapien

```
<220>
       <221> misc feature
       <222> (1)...(526)
       <223> n = A, T, C \text{ or } G
      <400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc
                                                                          60
ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta
                                                                         120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa
                                                                         180
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg
                                                                         240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa
                                                                         300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc
                                                                         360
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc
                                                                         420
acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa
                                                                         480
agttctataa actgtagtnt acttatttta atccccaaaq cacaqt
                                                                         526
      <210> 312
      <211> 500
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(500)
      \langle 223 \rangle n = A,T,C or G
      <400> 312
cetetetete eccaececet gaetetagag aactgggttt teteceagta etccagcaat
                                                                         60
tcatttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct
                                                                        120
ccatttetet ttecetteca cetgecagtt ttgetgacte teaacttgte atgagtgtaa
                                                                        180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg
                                                                        240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atcccctctt
                                                                        300
tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct
                                                                        360
tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct
                                                                        420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt
                                                                        480
tagtcttaat tatctattgg
                                                                        500
      <210> 313
      <211> 718
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(718)
      <223> n = A,T,C or G
      <400> 313
ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt gggaaggacc
                                                                         60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat
                                                                        120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa
                                                                        180
gtagtgacat gtttttgcac atttccagcc cttttaaata tccacacaca caggaagcac
                                                                        240
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga
                                                                        300
gcctcgccct gtgcctgntc ccgcttgtga gggaaggaca ttagaaaatg aattgatgtg
                                                                        360
ttccttaaag gatggcagga aaacagatcc tgttgtggat atttatttga acgggattac
                                                                        420
```

agatttgaaa tgaagtcaca aagtgagcat taccaatgag aggaaaacag acgagaaaat cttgatggt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc acgttatacca atcatttcta tttctaccct caaacaagct gtngaatatc tgacttacgg ttcttntggc ccacattttc atnatccacc cententtt aannttantc caaantgt <210> 314 <211> 358 <212> DNA <213> Homo sapien	480 540 600 660 718
<pre><400> 314 gtttatttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg gctctcggta gtccagcac tgtgaaacat gctccettta gattaacctc gtggacgctc ttgttgtatt gctgaactgt agtgccetgt attttgcttc tgtctgtgaa ttctgttgct tctggggcat ttccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt <210> 315 <211> 341</pre>	60 120 180 240 300 358
<212> DNA <213> Homo sapien <400> 315 taccacctcc ccgctggcac tgatgagggg catgagggg	60
gaccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac agtcaccage teceegacca geeggatate gteettaggg gteatgtagg etteetgaag tagettetge tgtaagaggg tgttgteecg ggggetegtg eggttattgg teetgggett gagggggegg tagatgeage acatggtgaa geagatgatg t	120 180 240 300 341
<210> 316 <211> 151 <212> DNA <213> Homo sapien <400> 316	
agactgggca agactcttac gccccacact gcaatttggt cttgttgccg tatccattta tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact cattcaggga gctctggttg caatattagt t	60 120 151
<211> 151 <212> DNA <213> Homo sapien	
<pre><400> 317 agaactagtg gatcctaatg aaatacctga aacatatatt ggcatttatc aatggctcaa atcttcattt atctctggcc ttaaccctgg ctcctgaggc tgcggccagc agatcccagg ccagggctct gttcttgcca cacctgcttg a </pre> <pre><210> 318</pre>	60 120 151
<210> 318 <211> 151 <212> DNA	

<213> Homo sapien	
<400> 318 actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcgga gggacctcct gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg tgggggcggt ttatcaggca gtgataaaca t	60 120 1 51
<210> 319 <211> 151 <212> DNA <213> Homo sapien	
<pre><400> 319 aactagtgga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg taagattggg tttatgtgat tttagtgggt a</pre>	60 120 151
<210> 320 <211> 150 <212> DNA <213> Homo sapien	
<pre><400> 320 aactagtgga tccactagtc cagtgtggtg gaattccatt gtgttggggt tctagatcgc gagcggctgc ccttttttt ttttttttt gggggggaatt tttttttt aatagttatt gagtgttcta cagcttacag taaataccat</pre>	60 120 150
<210> 321 <211> 151 <212> DNA <213> Homo sapien	
<400> 321 agcaactttg tttttcatcc aggttatttt aggcttagga tttcctctca cactgcagtt tagggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg tgcctctgag aaatcaaagt cttcatacac t	60 120 151
<210> 322 <211> 151 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(151) <223> n = A,T,C or G	
<pre><400> 322 atccagcatc ttctcctgtt tcttgccttc ctttttcttc ttcttasatt ctgcttgagg tttgggcttg gtcagtttgc cacagggctt ggagatggtg acagtcttct ggcattcggc attgtgcagg gctcgcttca nacttccagt t</pre>	60 120 151
<210> 323 <211> 151 <212> DNA	

```
<213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(151)
        <223> n = A,T,C or G
        <400> 323
  tgaggacttg tkttcttttt ctttattttt aatcctctta ckttgtaaat atattgccta
  nagactcant tactacccag tttgtggttt twtgggagaa atgtaactgg acagttagct
                                                                          60
  gttcaatyaa aaagacactt ancccatgtg g
                                                                         120
                                                                         151
        <210> 324
        <211> 461
        <212> DNA
        <213> Homo sapien
        <220>
       <221> misc_feature
       <222> (1)...(461)
       <223> n = A,T,C or G
       <400> 324
 acctgtgtgg aatttcagct ttcctcatgc aaaaggattt tgtatccccg gcctacttga
 agaagtggtc agctaaagga atccaggttg ttggttggac tgttaatacc tttgatgaaa
                                                                         60
 agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact
                                                                        120
 gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc
                                                                        180
 ctcatacagg gatatcaaaa taccctttgt gctacccagg ccctggggaa tcaggtgact
                                                                        240
 cacacaaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt
                                                                        300
 gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga
                                                                        360
 aaaaacgcac aagagcccct gccctgccct agctgangca c
                                                                        420
                                                                        461
       <210> 325
       <211> 400
       <212> DNA
       <213> Homo sapien
       <400> 325
acactgitte catgitatgt tietacaeat tgetacetea gigeteeigg aaacttaget
tttgatgtct ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcca
                                                                         60
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt
                                                                       120
tctataaatg aatgtgctga agcaaagtgc ccatggtggc ggcgaagaag agaaagatgt
                                                                       180
gttttgtttt ggactctctg tggtcccttc caatgctgtg ggtttccaac caggggaagg
                                                                       240
gtcccttttg cattgccaag tgccataacc atgagcacta cgctaccatg gttctgcctc
                                                                       300
                                                                       360
ctggccaagc aggctggttt gcaagaatga aatgaatgat
                                                                       400
      <210> 326
      <211> 1215
      <212> DNA
      <213> Homo sapien
      <400> 326
ggaggactgc agcccgcact cgcagccctg gcaggcggca ctggtcatgg aaaacgaatt
gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg tcagccgcac actgtttcca
                                                                        60
gaacteetae accateggge tgggeetgea cagtettgag geegaecaag ageeagggag
                                                                       120
                                                                       180
```

ccagatggtg	gaggccagcc	tctccgtacg	gcacccagag	tacaacagac	ccttgctcgc	240
taacgacctc	atgctcatca	agttggacga	atccgtgtcc	gagtctgaca	ccatccggag	300
catcagcatt	gcttcgcagt	gccctaccgc	ggggaactct	tgcctcgttt	ctggctgggg	360
tctgctggcg	aacggcagaa	tgcctaccgt	gctgcagtgc	gtgaacgtgt	cggtggtgtc	420
tgaggaggtc	tgcagtaagc	tctatgaccc	gctgtaccac	cccagcatgt	tctgcgccgg	480
cggagggcaa	gaccagaagg	actcctgcaa	cggtgactct	ggggggcccc	tgatctgcaa	540
		tgtctttcgg				600
aggtgtctac	accaacctct	gcaaattcac	tgagtggata	gagaaaaccg	tccaggccag	660
		cccatgaaat				720
tcaggaatat	ctgttcccag	cecetectee	ctcaggccca	ggagtccagg	ccccagccc	780
ctcctccctc	aaaccaaggg	tacagatccc	cagcccctcc	tccctcagac	ccaggagtcc	840
		cctcagaccc				900
ggagtccaga	cccccagcc	cctcctccct	cagacccagg	ggtccaggcc	cccaacccct	960
		ccaagccccc				1020
ggtcccagcc	cctcctccct	cagacccagc	ggtccaatgc	cacctagact	ctccctgtac	1080
		gttgacccaa				1140
ctttccccta	gatccagaaa	taaagtctaa	gagaagcgca	aaaaaaaaa	aaaaaaaaa	1200
aaaaaaaaa	aaaaa					1215

<210> 327

<211> 220

<212> PRT

<213> Homo sapien

<400> 327

Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val 25 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly 40 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu **5**5 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala 75 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp 85 90 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn 105 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro 120 125 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys 135 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly 150 155 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro 165 170 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala 185 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys 200 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser 210 215

<210> 328

WO 00/04149

```
<211> 234
        <212> DNA
        <213> Homo sapien
        <400> 328
  cgctcgtctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc
  agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc gtcctggtgc
                                                                           60
  atccgcagtg ggtgctgtca gccacacact gtttccagaa ctcctacacc atcgggctgg
                                                                          120
  gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca
                                                                         180
                                                                         234
        <210> 329
        <211> 77
        <212> PRT
        <213> Homo sapien
        <400> 329
 Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
                                      10
. Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
                                  25
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
                              40
                                                  45
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
                          55
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
 65
       <210> 330
       <211> 70
       <212> DNA
       <213> Homo sapien
       <400> 330
cccaacacaa tggcccgatc ccatccctga ctccgccctc aggatcgctc gtctctggta
                                                                         60
 gctgcagcca
                                                                         70
       <210> 331
       <211> 22
       <212> PRT
      <213> Homo sapien
      <400> 331
Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
                 5
                                     10
                                                         15
Val Ser Gly Ser Cys Ser
            20
      <210> 332
      <211> 2507
      <212> DNA
      <213> Homo sapien
      <400> 332
tggtgccgct gcagccggca gagatggttg agctcatgtt cccgctgttg ctcctccttc
tgcccttcct tctgtatatg gctgcgcccc aaatcaggaa aatgctgtcc agtggggtgt
                                                                        60
                                                                       120
```

gtacatcaac tgttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta 180 tcgggaagga gacagccaaa gagctggctc agagaggagc tcgagtatat ttagcttgcc 240 gggatgtgga aaagggggaa ttggtggcca aagagatcca gaccacgaca gggaaccagc 300 aggtgttggt gcggaaactg gacctgtctg atactaagtc tattcgagct tttgctaagg 360 gcttcttagc tgaggaaaag cacctccacg ttttgatcaa caatgcagga gtgatgatgt 420 gtccgtactc gaagacagca gatggctttg agatgcacat aggagtcaac cacttgggtc 480 acttcctcct aacccatctg ctgctagaga aactaaagga atcagcccca tcaaggatag 540 taaatgtgtc ttccctcgca catcacctgg gaaggatcca cttccataac ctgcagggcg 600 agaaattcta caatgcaggc ctggcctact gtcacagcaa gctagccaac atcctcttca 660 cccaggaact ggcccggaga ctaaaaggct ctggcgttac gacgtattct gtacaccctg 720 gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg tggtggcttt 780 tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac tgtgccttaa 840 cagaaggtot tgagattota agtgggaato atttcagtga ctgtcatgtg gcatgggtot 900 ctgcccaagc tegtaatgag actatagcaa ggcggctgtg ggacgtcagt tgtgacctgc 960 tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga ctgcagcaga 1020 ctacacagta cttcttgtca aaatgattct ccttcaaggt tttcaaaacc tttagcacaa 1080 agagagcaaa accttccagc cttgcctgct tggtgtccag ttaaaactca gtgtactgcc 1140 agattcgtct aaatgtctgt catgtccaga tttactttgc ttctgttact gccagagtta 1200 ctagagatat cataatagga taagaagacc ctcatatgac ctgcacagct cattttcctt 1260 ctgaaagaaa ctactaccta ggagaatcta agctatagca gggatgattt atgcaaattt 1320 gaactagett etttgtteac aatteagtte etcecaacea accagtette aetteaagag 1380 ggccacactg caacctcagc ttaacatgaa taacaaagac tggctcagga gcagggcttg 1440 cccaggcatg gtggatcacc ggaggtcagt agttcaagac cagcctggcc aacatggtga 1500 aaccccacct ctactaaaaa ttgtgtatat ctttgtgtgt cttcctgttt atgtgtgcca 1560 agggagtatt ttcacaaagt tcaaaacagc cacaataatc agagatggag caaaccagtg 1620 ccatccagtc tttatgcaaa tgaaatgctg caaagggaag cagattctgt atatgttggt 1680 aactacccac caagagcaca tgggtagcag ggaagaagta aaaaaagaga aggagaatac 1740 tggaagataa tgcacaaaat gaagggacta gttaaggatt aactagccct ttaaggatta 1800 actagttaag gattaatagc aaaagayatt aaatatgcta acatagctat ggaggaattg 1860 agggcaagca cccaggactg atgaggtctt aacaaaaacc agtgtggcaa aaaaaaaaa 1920 aaaaaaaaaa aaaaatccta aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa 1980 attatcttag ggactgatat tggtaattat ggtcaattta ataatatttt ggggcatttc 2040 cttacattgt cttgacaaga ttaaaatgtc tgtgccaaaa ttttgtattt tatttggaga 2100 cttcttatca aaagtaatgc tgccaaagga agtctaagga attagtagtg ttcccatcac 2160 ttgtttggag tgtgctattc taaaagattt tgatttcctg gaatgacaat tatattttaa 2220 ctttggtggg ggaaagagtt ataggaccac agtcttcact tctgatactt gtaaattaat 2280 cttttattgc acttgttttg accattaagc tatatgttta gaaatggtca ttttacggaa 2340 aaattagaaa aattotgata atagtgoaga ataaatgaat taatgtttta ottaatttat 2400 attgaactgt caatgacaaa taaaaattct ttttgattat tttttgtttt catttaccag 2460 aataaaaacg taagaattaa aagtttgatt acaaaaaaaa aaaaaaa 2507 <210> 333 <211> 3030 <212> DNA <213> Homo sapien <400> 333 gcaggcgact tgcgagctgg gagcgattta aaacgctttg gattcccccg gcctgggtgg 60 ggagagcgag ctgggtgccc cctagattcc ccgcccccgc acctcatgag ccgacctcg 120 gctccatgga gcccggcaat tatgccacct tggatggagc caaggatatc gaaggcttgc 180 tgggagcggg agggggggg aatctggtcg cccactcccc tctgaccagc cacccagcgg 240 cgcctacgct gatgcctgct gtcaactatg cccccttgga tctgccaggc tcggcggagc 300 cgccaaagca atgccaccca tgccctgggg tgccccaggg gacgtcccca gctcccgtgc 360 cttatggtta ctttggaggc gggtactact cctgccgagt gtcccggagc tcgctgaaac 420

cctgtgccca ggcagccacc ctggccgcgt accccgcgga gactcccacg gccggggaag

agtaccccag ycgccccact gagtttgcct tctatccggg atatccggga acctaccagc	
ctatggccag tracetggac gtgtctgtgg tgcagactct gggtgctcct ggagaaccgc	540
gacatgactc cctgttgcct gtggacagtt accagtcttg ggctctcgct ggagaaccgc acagccagat gtgttgccag ggagaacaga accagccagat gtgttgccag ggagaacaga accagcagaa	600
acagccagat gtgttgccag ggagaacaga acccaccagg tcccttttgg aaggcagcat ttgcagactc cagcgggcag caccttctg accactages	660
ttgcagactc cagegggcag cacecteetg acgeetgege etttegtege ggeegeaaga	720
aacgcattcc gtacagcaag gggcagttgc gggagctgga gcgggagtat gcggctaaca	780
agttcatcac caaggacaag aggcgcaaga tctcggcagc caccagcctc tcggagcgcc	840
	900
	960
gtcctgggga gaccaggaac ctgccaagcc caggctgggg ccaaggactc tgctgagagg cccctagaga caacacctt cccaggccac tggttggtg ggaggagcga aagtgggggt	1020
cccctagaga caacaccett cccaggecac tggctgctgg actgttectc aggageggcc	1080
	1140
cccaaagaac ctggcccagt cataatcatt catcctgaca gtggcaataa tcacgataac cagtactagc tgccatgatc gtragcctca tattataaca	1200
cagtactage tgecatgate gttagectea tattttetat etagagetet gtagageact ttagagaceg ettteatgag ttagagetaat tatgagetaa	1260
ttagaaaccg ctttcatgaa ttgagctaat tatgaataaa tttggaaggc gatccctttg	1320
cagggaaget tteteteaga ecceetteea ttacacetet caccetggta acageaggaa gactgaggaa aggggaacgg geagattegt tgtgtgggaaggaa acageaggaa	1380
gactgaggag aggggaacgg gcagattcgt tgtgtggctg tgatgtccgt ttagcatttt	1440
totoagotga cagotgggta ggtggacaat tgtagaggot gtotottoot cootcottgt	1500
ccaccccata gggtgtaccc actggtcttg gaagcaccca tccttaatac gatgattttt	1560
ctgtcgtgtg aaaatgaagc cagcaggctg cccctagtca gtccttcctt ccagagaaaa agagatttga gaaagtgcct gggtaattca ccattaatac	1620
agagatttga gaaagtgcct gggtaattca ccattaattt cctccccaa actctctgag	1680
tottcoctta atatttctgg tggttctgac caaagcaggt catggtttgt tgagcatttg	1740
ggatcccagt gaagtagatg tttgtagcct tgcatactta gcccttccca ggcacaaacg	1800
gagtggcaga gtggtgccaa ccctgttttc ccagtccacg tagacagatt cacagtgcgg	1860
aattetggaa getggagaca gaegggetet ttgeagagee gggaetetga gagggaeatg	1920
agggcctctg cctctgtgtt cattctctga tgtcctgtac ctgggctcag tgcccggtgg	1980
gactcatctc ctggccgcgc agcaaagcca gcgggttcgt gctggtcctt cctgcacctt	2040
aggetggggg tggggggeet geeggegeat tetecaegat tgagegeaca ggeetgaagt	2100
ctggacaacc cgcagaaccg aagctccgag cagcgggtcg gtggcgagta gtggggtcgg	2160
	2220
gccagetete etagaaacce egeggeggee geegeageea agtgtttatg geeegeggte	2280
gggtgggatc ctagccctgt ctcctctcct gggaaggagt gagggtggga cgtgacttag	2340
acacctacaa atctatttac caaagaggag cccgggactg agggaaaagg ccaaagagtg tgagtgcatg cggactgggg gttcaggga agaggagaaa	2400
tgagtgcatg cggactgggg gttcagggga agaggacgag gaggaggaag atgaggtcga	2460
tttcctgatt taaaaaaatcg tccaagcccc gtggtccagc ttaaggtcct cggttacatg	2520
cgccgctcag agcaggtcac tttctgcctt ccacgtcctc cttcaaggaa gccccatgtg	2580
ggtagctttc aatatcgcag gttcttactc ctctgcctct ataagctcaa acccaccaac gatcgggcaa gtaaacccc tccttgcgg agttagctct ataagctcaa acccaccaac	2640
	2700
gategggeaa gtaaacccc teettgeeg actteggaac tggegagagt teagegeaga ttggagagag gaaaaagge acaagaggg ctagagaggg geatggtgeg gggtgaccc	2760
ttggagagag gaaaaaggcc acaagaggg ctaggagg gcatggtgcg gggtgacccc	2820
	2880
	2940
aacaaaaaaa aaaaaaaaa aaaactcgag	3000
	3030
<210> 334	
<211> 2417	
<212> DNA	
212	

<213> Homo sapien

<400> 334

ggcggccgct ctagagctag tgggatcccc cgggctgcac gaattcggca cgagtgagtt ggagttttac ctgtattgtt ttaatttcaa caagcctgag gactagccac aaatgtaccc 60 agtttacaaa tgaggaaaca ggtgcaaaaa ggttgttacc tgtcaaaggt cgtatgtggc 120 agagccaaga tttgagccca gttatgtctg atgaacttag cctatgctct ttaaacttct 180 gaatgetgae cattgaggat atctaaactt agatcaattg catttteect ccaagactat 240 300

ttacttatca atacaataat accaccttta ccaatctatt gttttgatac gagactcaaa 360 tatgccagat atatgtaaaa gcaacctaca agctctctaa tcatgctcac ctaaaagatt 420 cccgggatct aataggctca aagaaacttc ttctagaaat ataaaagaga aaattggatt 480 atgcaaaaat tcattattaa tttttttcat ccatccttta attcagcaaa catttatctg 540 ttgttgactt tatgcagtat ggccttttaa ggattggggg acaggtgaag aacggggtgc 600 cagaatgcat cctcctacta atgaggtcag tacacatttg cattttaaaa tgccctgtcc 660 agctgggcat ggtggatcat gcctgtaatc tcaacattgg aaggccaagg caggaggatt 720 gcttcagccc aggagttcaa gaccagcctg ggcaacatag aaagacccca tctctcaatc 780 aatcaatcaa tgccctgtct ttgaaaataa aactctttaa gaaaggttta atgggcaggg 840 tgtggtagct catgcctata atacagcact ttgggaggct gaggcaggag gatcacttta 900 gcccagaagt tcaagaccag cctgggcaac aagtgacacc tcatctcaat tttttaataa 960 aatgaataca tacataagga aagataaaaa gaaaagttta atgaaagaat acagtataaa 1020 acaaatctct tggacctaaa agtatttttg ttcaagccaa atattgtgaa tcacctctct 1080 gtgttgagga tacagaatat ctaagcccag gaaactgagc agaaagttca tgtactaact 1140 aatcaacccg aggcaaggca aaaatgagac taactaatca atccgaggca aggggcaaat 1200 tagacggaac ctgactctgg tctattaagc gacaactttc cctctgttgt attttcttt 1260 tattcaatgt aaaaggataa aaactctcta aaactaaaaa caatgtttgt caggagttac 1320 aaaccatgac caactaatta tggggaatca taaaatatga ctgtatgaga tcttgatggt 1380 ttacaaagtg tacccactgt taatcacttt aaacattaat gaacttaaaa atgaatttac 1440 ggagattgga atgittetti eetgitgiat tagitggete aggetgeeat aacaaaatae 1500 cacagactgg gaggettaag taacagaaat teatttetea cagttetggg ggetggaagt 1560 ccacgatcaa ggtgcaggaa aggcaggctt cattctgagg cccctctctt ggctcacatg 1620 tggccaccct cccactgcgt gctcacatga cctctttgtg ctcctggaaa gagggtgtgg 1680 gggacagagg gaaagagaag gagagggaac tctctggtgt ctcgtctttc aaggacccta 1740 acctgggcca ctttggccca ggcactgtgg ggtgggggt tgtggctgct ctgctctgag 1800 tggccaagat aaagcaacag aaaaatgtcc aaagctgtgc agcaaagaca agccaccgaa 1860 cagggatetg eteateagtg tggggacete caagteggee accetggagg caageececa 1920 cagageceat geaaggtgge ageageagaa gaagggaatt gteeetgtee ttggeacatt 1980 cctcaccgac ctggtgatgc tggacactgc gatgaatggt aatgtggatg agaatatgat 2040 ggactcccag aaaaggagac ccagctgctc aggtggctgc aaatcattac agccttcatc 2100 ctggggagga actgggggcc tggttctggg tcagagagca gcccagtgag ggtgagagct 2160 acagectgte etgecagetg gatececagt eceggteaac cagtaateaa ggetgageag 2220 atcaggette eeggagetgg tettgggaag eeageeetgg ggtgagttgg eteetgetgt 2280 ggtactgaga caatattgtc ataaattcaa tgcgcccttg tatccctttt tctttttat 2340 ctgtctacat ctataatcac tatgcatact agtctttgtt agtgtttcta ttcmacttaa 2400 tagagatatg ttatact 2417

<210> 335

<211> 2984

<212> DNA

<213> Homo sapien

<400> 335

atccctcctt ccccactctc ctttccagaa ggcacttggg gtcttatctg ttggactctg 60 aaaacacttc aggcgccctt ccaaggcttc cccaaacccc taagcagccg cagaagcgct 120 cccgagctgc cttctcccac actcaggtga tcgagttgga gaggaagttc agccatcaga 180 agtacctgtc ggcccctgaa cgggcccacc tggccaagaa cctcaagctc acggagaccc 240 aagtgaagat atggttccag aacagacgct ataagactaa gcgaaagcag ctctcctcgg 300 agctgggaga cttggagaag cactcctctt tgccggccct gaaagaggag gccttctccc 360 gggcctccct ggtctccgtg tataacagct atccttacta cccatacctg tactgcgtgg 420 gcagctggag cccagctttt tggtaatgcc agctcaggtg acaaccatta tgatcaaaaa 480 ctgccttccc cagggtgtct ctatgaaaag cacaaggggc caaggtcagg gagcaagagg 540 tgtgcacacc aaagctattg gagatttgcg tggaaatctc asattcttca ctggtgagac 600 aatgaaacaa cagagacagt gaaagtttta atacctaagt cattccccca gtgcatactg 660 taggtcattt tttttgcttc tggctacctg tttgaagggg agagagggaa aatcaagtgg 720

WO 00/04149 PCT/US99/15838

tattttccag cactttgtat gattttggat gagctgtaca cccaaggatt ctgttctgca 780 actccatcct cctgtgtcac tgaatatcaa ctctgaaaga gcaaacctaa caggagaaaag 840 gacaaccagg atgaggatgt caccaactga attaaactta agtccagaag cctcctgttg 900 gccttggaat atggccaagg ctctctctgt ccctgtaaaa gagaggggca aatagagagt ctccaagaga acgeeeteat geteageaea tatttgeatg ggagggggag atgggtggga 960 1020 ggagatgaaa atatcagctt ttcttattcc tttttattcc ttttaaaaatg gtatgccaac 1080 ttaagtattt acagggtggc ccaaatagaa caagatgcac tcgctgtgat tttaagacaa 1140 gctgtataaa cagaactcca ctgcaagagg gggggccggg ccaggagaat ctccgcttgt 1200 ccaagacagg ggcctaagga gggtctccac actgctgcta ggggctgttg catttttta 1260 ttagtagaaa gtggaaaggc ctcttctcaa cttttttccc ttgggctgga gaatttagaa 1320 tcagaagttt cctggagttt tcaggctatc atatacactg tatcctgaaa ggcaacataa 1380 ttcttccttc cctcctttta aaattttgtg ttcctttttg cagcaattac tcactaaagg 1440 gcttcatttt agtccagatt tttagtctgg ctgcacctaa cttatgcctc gcttatttag 1500 cccgagatct ggtcttttt tttttttt tttttccgtc tccccaaagc tttatctgtc 1560 ttgacttttt aaaaaagttt gggggcagat tctgaattgg ctaaaagaca tgcatttta aaactagcaa ctcttatttc tttcctttaa aaatacatag cattaaatcc caaatcctat 1620 ttaaagacct gacagcttga gaaggtcact actgcattta taggaccttc tggtggttct 1680 gctgttacgt ttgaagtctg acaatccttg agaatctttg catgcagagg aggtaagagg 1740 1800 tattggattt tcacagagga agaacacagc gcagaatgaa gggccaggct tactgagctg 1860 tccagtggag ggctcatggg tgggacatgg aaaagaaggc agcctaggcc ctggggagcc 1920 cagtccactg agcaagcaag ggactgagtg agccttttgc aggaaaaggc taagaaaaag gaaaaccatt ctaaaacaca acaagaaact gtccaaatgc tttgggaact gtgtttattg 1980 2040 cctataatgg gtccccaaaa tgggtaacct agacttcaga gagaatgagc agagagcaaa 2100 ggagaaatet ggetgteett ecatttteat tetgttatet eaggtgaget ggtagaggg 2160 agacattaga aaaaaatgaa acaacaaaac aattactaat gaggtacgct gaggcctggg 2220 agtototiga otocactact taattoogtt tagtgagaaa cotttoaatt trottttatt 2280 agaagggcca gcttactgtt ggtggcaaaa ttgccaacat aagttaatag aaagttggcc 2340 aatttcaccc cattttctgt ggtttgggct ccacattgca atgttcaatg ccacgtgctg 2400 ctgacaccga ccggagtact agccagcaca aaaggcaggg tagcctgaat tgctttctgc 2460 totttacatt tottttaaaa taagcattta gtgotcagto cotactgagt actotttoto 2520 teceeteete tgaatttaat tettteaact tgeaatttge aaggattaca cattteactg 2580 tgatgtatat tgtgttgcaa aaaaaaaaa aagtgtcttt gtttaaaatt acttggtttg 2640 tgaatccatc ttgctttttc cccattggaa ctagtcatta acccatctct gaactggtag 2700 aaaaacatct gaagagctag tctatcagca tctgacaggt gaattggatg gttctcagaa 2760 ccatttcacc cagacageet gtttetatee tgtttaataa attagtttgg gttetetaca 2820 tgcataacaa accetgetee aatetgteae ataaaagtet gtgaettgaa gtttagteag cacccccacc aaactttatt tttctatgtg ttttttgcaa catatgagtg ttttgaaaat 2880 2940 2984

<210> 336

<211> 147

<212> PRT

<213> Homo sapien

<400> 336

 Pro
 Ser
 Phe
 Pro
 Thr
 Leu
 Leu
 Ser
 Arg
 Arg
 His
 Leu
 Gly
 Ser
 Tyr
 Leu

 Leu
 Asp
 Ser
 Glu
 Asn
 Thr
 Ser
 Gly
 Ala
 Leu
 Pro
 Arg
 Leu
 Pro
 Arg
 Leu
 Pro
 Arg
 Arg
 Arg
 Ala
 Ala
 Ala
 Phe
 Ser
 His
 Thr
 Gln
 Gln
 Arg
 Ala
 Arg
 Ala
 Ala
 Ala
 Phe
 Ser
 His
 Gln
 Leu
 Ser
 Ala

 Val
 Ile
 Glu
 Leu
 Glu
 Arg
 Lys
 Phe
 Ser
 His
 Gln
 Lys
 Arg
 Ala
 Ala
 Ala
 Ala
 Ala
 Ileu
 Thr
 Gln
 Ala
 Ala

Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln 85 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala 105 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn 120 125 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro 135 Ala Phe Trp 145 <210> 337 <211> 9 <212> PRT <213> Homo sapien <400> 337 Ala Leu Thr Gly Phe Thr Phe Ser Ala <210> 338 <211> 9 <212> PRT <213> Homo sapien <400> 338 Leu Leu Ala Asn Asp Leu Met Leu Ile 5 <210> 339 <211> 318 <212> PRT <213> Homo sapien <400> 339 Met Val Glu Leu Met Phe Pro Leu Leu Leu Leu Leu Pro Phe Leu 10 5 Leu Tyr Met Ala Ala Pro Gln Ile Arg Lys Met Leu Ser Ser Gly Val Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Thr Gly Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg 55 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu 75 Val Ala Lys Glu Ile Gln Thr Thr Gly Asn Gln Gln Val Leu Val 90 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys 105 100 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala 120 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met 135 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu

```
145
                       150
                                            155
  Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser
                   165
                                       170
  Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
                                   185
  Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
                               200
  Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly
                                                   205
                          215
  Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val
                      230
                                           235
  Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe
                  245
                                       250
  Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu
                                  265
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His
                              280
 Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg
                          295
                                               300
 Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp
                      310
       <210> 340
       <211> 483
       <212> DNA
       <213> Homo sapien
       <400> 340
 gccgaggtct gccttcacac ggaggacacg agactgcttc ctcaagggct cctgcctgcc
 tggacactgg tgggaggcgc tgtttagttg gctgttttca gaggggtctt tcggagggac
                                                                         60
 ctcctgctgc aggctggagt gtctttattc ctggcgggag accgcacatt ccactgctga
                                                                        120
ggttgtgggg gcggtttatc aggcagtgat aaacataaga tgtcatttcc ttgactccgg
                                                                        180
cetteaattt tetetttgge tgacgaegga gteegtggtg teeegatgta actgaceeet
                                                                        240
gctccaaacg tgacatcact gatgctcttc tcgggggtgc tgatggcccg cttggtcacg
                                                                        300
tgctcaatct cgccattcga ctcttgctcc aaactgtatg aagacacctg actgcacgtt
                                                                        360
ttttctgggc ttccagaatt taaagtgaaa ggcagcactc ctaagctccg actccgatgc
                                                                        420
                                                                        480
ctg
                                                                        483
      <210> 341
      <211> 344
      <212> DNA
      <213> Homo sapien
      <400> 341
ctgctgctga gtcacagatt tcattataaa tagcctccct aaggaaaata cactgaatgc
tatttttact aaccattcta tttttataga aatagctgag agtttctaaa ccaactctct
                                                                        60
gctgccttac aagtattaaa tattttactt ctttccataa agagtagctc aaaatatgca
                                                                       120
attaatttaa taatttctga tgatggtttt atctgcagta atatgtatat catctattag
                                                                       180
aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc
                                                                       240
ctgattctta acattgtctt taatgaccac aagacaacca acag
                                                                       300
                                                                       344
      <210> 342
      <211> 592
      <212> DNA
```

<213> Homo sapien

```
<400> 342
acagcaaaaa agaaactgag aagcccaaty tgctttcttg ttaacatcca cttatccaac
                                                                        60
caatgtggaa acttcttata cttggttcca ttatgaagtt ggacaattgc tgctatcaca
                                                                       120
cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg
                                                                       180
accaggattg gaattttata aaaatattgt tgatgggaag ttgctaaagg gtgaattact
                                                                       240
tccctcagaa gagtgtaaag aaaagtcaga gatgctataa tagcagctat tttaattggc
                                                                       300
aagtgccact gtggaaagag ttcctgtgtg tgctgaagtt ctgaagggca gtcaaattca
                                                                       360
tcagcatggg ctgtttggtg caaatgcaaa agcacaggtc tttttagcat gctggtctct
                                                                       420
cccgtgtcct tatgcaaata atcgtcttct tctaaatttc tcctaggctt cattttccaa
                                                                       480
agttcttctt ggtttgtgat gtcttttctg ctttccatta attctataaa atagtatggc
                                                                       540
ttcagccacc cactettege ettagettga cegtgagtet eggetgeege tg
                                                                       592
      <210> 343
      <211> 382
      <212> DNA
      <213> Homo sapien
      <400> 343
ttcttgacct cctcctcctt caagctcaaa caccacctcc cttattcagg accggcactt
                                                                        60
cttaatgttt gtggctttct ctccagcctc tcttaggagg ggtaatggtg gagttggcat
                                                                       120
cttgtaactc tcctttctcc tttcttcccc tttctctgcc cgcctttccc atcctgctgt
                                                                       180
agacttettg attgtcagte tgtgtcacat ccagtgattg ttttggttte tgttcccttt
                                                                       240
ctgactgccc aaggggctca gaaccccagc aatcccttcc titcactacc tictititig
                                                                       300
ggggtagttg gaagggactg aaattgtggg gggaaggtag gaggcacatc aataaagagg
                                                                       360
aaaccaccaa gctgaaaaaa aa
                                                                       382
      <210> 344
      <211> 536
      <212> DNA
      <213> Homo sapien
      <400> 344
ctgggcctga agctgtaggg taaatcagag gcaggcttct gagtgatgag agtcctgaga
                                                                        60
caataggcca cataaacttg gctggatgga acctcacaat aaggtggtca cctcttgttt
                                                                       120
gtttaggggg atgccaagga taaggccagc tcagttatat gaagagaagc agaacaaaca
                                                                       180
agtotttcag agaaatggat gcaatcagag tgggatcccg gtcacatcaa ggtcacactc
                                                                       240
caccttcatg tgcctgaatg gttgccaggt cagaaaaatc cacccttac gagtgcggct
                                                                       300
tegacectat atececegee egegteeett tetecataaa attettetta gtagetatta
                                                                       360
cottettatt attigateta gaaatigeee teetittaee eetaceatga geeetacaaa
                                                                       420
caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa
                                                                       480
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa
                                                                       536
      <210> 345
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 345
accttttgag gtctctctca ccacctccac agccaccgtc accgtgggat gtgctggatg
                                                                        60
tgaatgaagc ccccatcttt gtgcctcctg aaaagagagt ggaagtgtcc gaggactttg
                                                                       120
gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga
                                                                       180
aaataacata toggatttgg agagacactg coaactggot ggagattaat coggacactg
                                                                       240
                                                                       251
gtgccatttc c
```

```
<210> 346
         <211> 282
         <212> DNA
         <213> Homo sapien
         <220>
         <221> misc_feature
         <222> (1)...(282)
         <223> n = A,T,C or G
  <400> 346
  cgcgtctctg acactgtgat catgacaggg gttcaaacag aaagtgcctg ggccctcctt
  ctaagtcttg ttaccaaaaa aaggaaaaag aaaagatctt ctcagttaca aattctggga
                                                                           60
  agggagacta tacctggctc ttgccctaag tgagaggtct tccctcccgc accaaaaaat
                                                                          120
  agaaaggctt tctatttcac tggcccaggt agggggaagg agagtaactt tgagtctgtg
                                                                          180
  ggtctcattt cccaaggtgc cttcaatgct catnaaaacc aa
                                                                          240
                                                                          282
        <210> 347
        <211> 201
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(201)
        <223> n = A, T, C \text{ or } G
        <400> 347
 acacacataa tattataaaa tgccatctaa ttggaaggag ctttctatca ttgcaagtca
 taaatataac ttttaaaana ntactancag cttttaccta ngctcctaaa tgcttgtaaa
                                                                          60
 tetgagaetg aetggaecca eccagaecca gggeaaagat acatgttace atateatett
                                                                         120
 tataaagaat tttttttgt c
                                                                         180
                                                                         201
       <210> 348
       <211> 251
       <212> DNA
       <213> Homo sapien
       <400> 348
ctgttaatca caacatttgt gcatcacttg tgccaagtga gaaaatgttc taaaatcaca
agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgcccctg ggcaggcaga
                                                                          60
aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg
                                                                        120
ggggaaggtt ttattataga actoccaaca goccacotca otoctgccac ccaccogatg
                                                                        180
                                                                        240
                                                                        251
       <210> 349
       <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 349
taaaaatcaa gccatttaat tgtatctttg aaggtaaaca atatatggga gctggatcac
aacccctgag gatgccagag ctatgggtcc agaacatggt gtggtattat caacagagtt
                                                                         60
cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt
                                                                        120
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca
                                                                        180
                                                                        240
```

actcctggtt t 251 <210> 350 <211> 908 <212> DNA <213> Homo sapien <400> 350 ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt 60 agcccgcccg gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac 120 cggctggaat tgctctggtt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180 cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240 gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300 tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tggtgtcaga 360 aggatcatgt gccacagtcc atgaaggctc tggagaaact agtcaaaagg agacatccac 420 ctgtgatatt tgccagtttg gtgcagaatg tgacgaagat gccgaggatg tctggtgtgt 480 gtgtaatatt gactgttctc aaaccaactt caatcccctc tgcgcttctg atgggaaatc 540 ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt 600 catgictitg ggtcgatgtc aagataacac aactacaact actaagtctg aagatgggca 660 ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca 720 ccacatacct tgtccggaac attacaatgg cttctgcatg catgggaagt gtgagcattc 780 tatcaatatg caggagccat cttgcaggtg tgatgctggt tatactggac aacactgtga 840 aaaaaaggac tacagtgttc tatacgttgt tcccggtcct gtacgatttc agtatgtctt 900 aatcgcag 908 <210> 351 <211> 472 <212> DNA <213> Homo sapien <400> 351 ccagttattt gcaagtggta agagcctatt taccataaat aatactaaga accaactcaa 60 gtcaaacctt aatgccattg ttattgtgaa ttaggattaa gtagtaattt tcaaaattca 120 cattaacttg attttaaaat cagwtttgyg agtcatttac cacaagctaa atgtgtacac 180 tatgataaaa acaaccattg tattcctgtt tttctaaaca gtcctaattt ctaacactgt 240 atatatcctt cgacatcaat gaactttgtt ttcttttact ccagtaataa agtaggcaca 300 gatetgteca caacaaactt geeetetat geettgeete teaceatget etgetecagg 360 tcagccccct tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg 420 gtaatatata tttagggaag atgttgcttt gcccacacac gaagcaaagt aa 472 <210> 352 <211> 251 <212> DNA <213> Homo sapien <400> 352 ctcaaagcta atctctcggg aatcaaacca gaaaagggca aggatcttag gcatggtgga 60 tgtggataag gccaggtcaa tggctgcaag catgcagaga aagaggtaca tcggagcgtg 120 caggetgegt teegteetta egatgaagae caegatgeag tttecaaaea ttgecaetae 180 atacatggaa aggagggga agccaaccca gaaatgggct ttctctaatc ctgggatacc 240 aataagcaca a 251 <210> 353 <211> 436 <212> DNA

120

<213> Homo sapien

<400> 353 tttttttttt ttttttttt ttttttacaa caatgcagtc atttatttat tgagtatgtg cacattatgg tattattact atactgatta tatttatcat gtgacttcta attaraaaat 60 gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata gacattaaca 120 gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tgggaaatga 180 gggggacaaa tggaagccar atcaaatttg tgtaaaacta ttcagtatgt ttcccttgct 240 tcatgtctga raaggctctc ccttcaatgg ggatgacaaa ctccaaatgc cacacaaatg 300 ttaacagaat actagattca cactggaacg ggggtaaaga agaaattatt ttctataaaa 360 gggctcctaa tgtagt 420 436 <210> 354 <211> 854 <212> DNA <213> Homo sapien <400> 354 ccttttctag ttcaccagtt ttctgcaagg atgctggtta gggagtgtct gcaggaggag caagtetgaa accaaateta ggaaacatag gaaacgagee aggeacaggg etggtgggee 60 atcagggacc accetttggg ttgatatttt gettaatetg catettttga gtaagateat 120 ctggcagtag aagctgttct ccaggtacat ttctctagct catgtacaaa aacatcctga 180 aggactttgt caggtgcctt gctaaaagcc agatgcgttc ggcacttcct tggtctgagg 240 ttaattgcac acctacaggc actgggctca tgctttcaag tattttgtcc tcactttagg 300 gtgagtgaaa gatccccatt ataggagcac ttgggagaga tcatataaaa gctgactctt 360 gagtacatgc agtaatgggg tagatgtgtg tggtgtgtct tcattcctgc aagggtgctt 420 gttagggagt gtttccagga ggaacaagtc tgaaaccaat catgaaataa atggtaggtg 480 tgaactggaa aactaattca aaagagagat cgtgatatca gtgtggttga tacaccttgg 540 caatatggaa ggctctaatt tgcccatatt tgaaataata attcagcttt ttgtaataca 600 aaataacaaa ggattgagaa tcatggtgtc taatgtataa aagacccagg aaacataaat 550 atatcaactg cataaatgta aaatgcatgt gacccaagaa ggccccaaag tggcagacaa 720 cattgtaccc attttccctt ccaaaatgtg agcggcgggc ctgctgcttt caaggctgtc 780 acacgggatg tcag 840 854 <210> 355 <211> 676 <212> DNA <213> Homo sapien <400> 355 gaaattaagt atgagctaaa ttccctgtta aaacctctag gggtgacaga tctcttcaac caggicaaag cigatcitic iggaatgica ccaaccaagg gcctatatti atcaaaagcc 60 atccacaagt catacctgga tgtcagcgaa gagggcacgg aggcagcagc agccactggg 120 gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccaccccttc 180 ctgttcttta taaggcacac tcataccaac acgatcctat tctgtggcaa gcttgcctct 240 ccctaatcag atggggttga gtaaggctca gagttgcaga tgaggtgcag agacaatcct 300 gtgactttcc cacggccaaa aagctgttca cacctcacgc acctctgtgc ctcagtttgc 360 tcatctgcaa aataggtcta ggatttcttc caaccatttc atgagttgtg aagctaaggc 420 tttgttaatc atggaaaaag gtagacttat gcagaaagcc tttctggctt tcttatctgt 480 ggtgtctcat ttgagtgctg tccagtgaca tgatcaagtc aatgagtaaa attttaaggg 540 attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgacc tgacatctct 600 gcttaaagaa aaccag 660

<210> 356

<211> 574

<212> DNA <213> Homo sapien <400> 356 tttttttttt tttttcagga aaacattctc ttactttatt tgcatctcag caaaggttct 60 catgtggcac ctgactggca tcaaaccaaa gttcgtaggc caacaaagat gggccactca 120 caagetteec atttgtagat eteagtgeet atgagtatet gacacetgtt cetetetea 180 gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc 240 aaaagtccac aaaactgcag tetttgctgg gatagtaagc caagcagtgc ctggacagca 300 gagttetttt ettgggeaac agataaccag acaggaetet aategtgete ttatteaaca 360 ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acagggaagg 420 agatacaage tegittacat gigatagate taacaaagge atetacegaa gietggietg 480 gatagacggc acagggagct cttaggtcag cgctgctggt tggaggacat tcctgagtcc 540 agctttgcag cctttgtgca acagtacttt ccca 574 <210> 357 <211> 393 <212> DNA <213> Homo sapien <400> 357 ttttttttt ttttttttt tacagaatat aratgcttta tcactgkact 60 taatatggkg kettgtteae tataettaaa aatgeaceae teataaatat ttaatteage 120 aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaag 180 atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240 araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300 gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct 360 tttttttctt tttctgtttt tttttttt tac 393 <210> 358 <211> 630 <212> DNA <213> Homo sapien <400> 358 acagggtaaa caggaggatc cttgctctca cggagcttac attctagcag gaggacaata 60 ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga 120 gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg 180 gagtttaaac tgagagaagc aagtgcttaa actgaaggat gtgttgaaga agaagggaga 240 gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact 300 gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag 360 attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa 420 tcactgaagg gagtaatgtg acattacttt tcacttcagg atggccattc taactccagg 480 gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt 540 gaaagacaaa aataagtggg gaaattcagg ggatagtgaa aatcagtagg acttaatgag 600 caagccagag gttcctccac aacaaccagt 630 <210> 359 <211> 620 <212> DNA <213> Homo sapien <400> 359 acagcattcc aaaatataca tctagagact aarrgtaaat gctctatagt gaagaagtaa 60 taattaaaaa atgctactaa tatagaaaat ttataatcag aaaaataaat attcagggaq 120

ctcaccagaa gaataaagtg ctctgccagt tattaaaagt	
ctcaccagaa gaataaagtg ctctgccagt tattaaagga ttactgctgg tgaattaaat atggcattcc ccaagggaaa tagagagatt cttctggatt atgttcaata tttatttcac aggattaact gttttaggaa cagataraaa ggttggaaa	180
aggattaact gttttaggaa cagatataaa gcttcgccac ggaagagatg gacaaagcac aaagacaaca tgatacctta ggaagcaaca ctacccttta aggaagagatg gacaaagcac	240
aaagacaaca tgatacctta ggaagcaaca ctaccctttc aggcataaaa tttggagaaa	300
tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt aatgtaagat aactttataa gaattctggg tcaaataaaa baata	360
aatgtaagat aactttataa gaattetggg teaaataaaa ttetttgaag aaaacateea aatgteattg acttateaaa tactatetta geatataaaa teetttgaag aaaacateea	420
aatgtcattg acttatcaaa tactatcttg gcatataaac tatgaaggca aaactaaaca aacaaaaagc tcacaccaaa caaaaccatc aacttatta	480
aacaaaaagc tcacaccaaa caaaaccatc aacttatttt gtattctata acatacgaga ctgtaaagat gtgacagtgt	540
ctgtaaagat gtgacagtgt	600 630
<210> 360	620
<211> 431	
<212> DNA	
<213> Homo sapien	
<400> 360	
aaaaaaaaa agccagaaca acatgtgata gataatatga ttggctgcac acttccagac	
tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa tactcatcat ttttggccag cagttgtttg atcaccaaag atcaccaaa	60
tactcatcat tittggccag cagttgtttg atcaccaaac atcatgccag aatactcagc aaaccttctt agctcttgag aagtcaaagt ccgggggaat thanks	120
aaaccttctt agctcttgag aagtcaaagt ccgggggaat ttattcctgg caattttaat	180
tggactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgtcact agtggacatg cagtggcaga gctcctggta accaggtaga	240
agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg tgatgccaag cgtgacacct gtagcactca aatttgtata	300 360
tgatgccaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcggtgtgt	420
	431
<210> 361	
<211> 351	
<212> DNA	
<213> Homo sapien	
<400> 361	
acactgattt Ccgatcaaaa goobaac	
acactgattt ccgatcaaaa gaatcatcat ctttaccttg acttttcagg gaattactga	60
actttcttct cagaagatag ggcacagcca ttgccttggc ctcacttgaa gggtctgcat	120
ttgacttcct ccgqqqcttt cccqaqqqt tagactactcg agggagaaat atcgggaggt	180
caatcotgga ttcaatgtot gaaacgtoga tabatagggg cottgoggco ctcagggotg	240
ctgccactct gtcctccage tetgacaget ceteatetgt ggtcetgttg t	300
	351
<210> 362	
<211> 463	
<212> DNA	
<213> Homo sapien	
<400> 362	
acttcatcag gccataatgg gtgcctcggg tgagge	
acttcatcag gccataatgg gtgcctcccg tgagaatcca agcacctttg gactgcgcga tgtagatgag ccggctgaag atcttgcgca tgcgcggctt cagggcgaag ttcttggcgc	60
ccccggtcac agaaatgacc aggttgggta therease cagggcgaag ttcttggcgc	120
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttccct ttcttcccca gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa atacttccct ttcttcccca	180
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttccttggtg tgtttcttgt	240
agttccattt ctcactttgg ttgatctggg tgccttccat gtgctggctc tgggcatagc	300
cacacttgca cacattetee etgataagea egatggtgtg gacaggaagg aaggatttea	360
ttgageetge ttatggaaac tggtattgtt agettaaata gae	420
<210> 363	463

<211> 653

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(653)
      <223> n = A,T,C or G
      <400> 363
acccccgagt ncctgnctgg catactgnga acgaccaacg acaccccaa gctcggcctc
                                                                        60
ctcttggnga ttctgggtga catcttcatg aatggcaacc gtgccagwga ggctgtcctc
                                                                       120
tgggaggcac tacgcaagat gggactgcgt cctggggtga gacatcctct ccttggagat
                                                                       180
ctaacgaaac ttctcaccta tgagttgtaa agcagaaata cctgnactac agacgagtgc
                                                                       240
ccaacagcaa cccccggaa gtatgagttc ctctrgggcc tccgttccta ccatgagasc
                                                                       300
tagcaagatg naagtgttga gantcattgc agaggttcag aaaagagacc cntcgtgact
                                                                       360
ggtctgcaca gttcatggag gctgcagatg aggccttgga tgctctggat gctgctgcag
                                                                       420
ctgaggccga agcccgggct gaagcaagaa cccgcatggg aattggagat gaggctgtgt
                                                                       480
ntgggccctg gagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag
                                                                       540
attttggaga tccntggtcc agaattccat ttaccttctg ggccagatac caccagaatg
                                                                       600
cocgetecag atteceteag acetttgeeg gteceattat tggtestggt ggt
                                                                       653
      <210> 364
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 364
actagaggaa agacgttaaa ccactctact accacttgtg gaactctcaa agggtaaatg
                                                                        60
acaaagccaa tgaatgactc taaaaaacaat atttacattt aatggtttgt agacaataaa
                                                                       120
aaaacaaggt ggatagatct agaattgtaa cattttaaga aaaccatagc atttgacaga
                                                                       180
tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata
                                                                       240
catttcacac ccttcatata aattcactat cttggcttga ggcactccat aaaatgtatc
                                                                       300
acgtgcatag taaatcttta tatttgctat ggcgttgcac tagaggactt ggactgcaac
                                                                       360
aagtggatgc gcggaaaatg aaatcttctt caatagccca g
                                                                       401
      <210> 365
      <211> 356
      <212> DNA
      <213> Homo sapien
      <400> 365
ccagtgtcat atttgggctt aaaatttcaa gaagggcact tcaaatggct ttgcatttgc
                                                                        60
atgtttcagt gctagagcgt aggaatagac cctggcgtcc actgtgagat gttcttcagc
                                                                       120
taccagagca tcaagtctct gcagcaggtc attcttgggt aaagaaatga cttccacaaa
                                                                       180
ctctccatcc cctggctttg gcttcggcct tgcgttttcg gcatcatctc cgttaatggt
                                                                       240
gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga
                                                                       300
acatteggea atgreecett tgtagecagt ttettetteg ageteeegga gageag
                                                                       356
      <210> 366
      <211> 1851
      <212> DNA
      <213> Homo sapien
      <400> 366
tcatcaccat tgccagcagc ggcaccgtta gtcaggtttt ctgggaatcc cacatgagta
                                                                        60
```

```
cttccgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt
   tcacttcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga
                                                                          120
   ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg
                                                                          180
   caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag
                                                                          240
   aagatacatc aacattttgc tcaagtagag ggctgactat acttgctgat ccacaacata
                                                                          300
   cagcaagtat gagagcagtt cttccatatc tatccagcgc atttaaattc gctttttct
                                                                          360
   tgattaaaaa tttcaccact tgctgttttt gctcatgtat accaagtagc agtggtgtga
                                                                          420
  ggccatgctt gttttttgat tcgatatcag caccgtataa gagcagtgct ttggccatta
                                                                          480
  atttatcttc attgtagaca gcatagtgta gagtggtatt tccatactca tctggaatat
                                                                          540
  ttggatcagt gccatgttcc agcaacatta acgcacattc atcttcctgg cattgtacgg
                                                                          600
  cctttgtcag agctgtcctc tttttgttgt caaggacatt aagttgacat cgtctgtcca
                                                                         660
  gcacgagttt tactacttct gaattcccat tggcagaggc cagatgtaga gcagtcctct
                                                                         720
  tttgcttgtc cctcttgttc acatccgtgt ccctgagcat gacgatgaga tcctttctgg
                                                                         780
  ggactttacc ccaccaggca gctctgtgga gcttgtccag atcttctcca tggacgtggt
                                                                         840
  acctgggatc catgaaggcg ctgtcatcgt agtctcccca agcgaccacg ttgctcttgc
                                                                         900
  cgctcccctg cagcagggga agcagtggca gcaccacttg cacctcttgc tcccaagcgt
                                                                         960
  cttcacagag gagtcgttgt ggtctccaga agtgcccacg ttgctcttgc cgctcccct
                                                                        1020
  gtccatccag ggaggaagaa atgcaggaaa tgaaagatgc atgcacgatg gtatactcct
                                                                        1080
  cagccatcaa acttctggac agcaggtcac ttccagcaag gtggagaaag ctgtccaccc
                                                                        1140
  acagaggatg agatecagaa accaeaatat ecatteacaa acaaacaett tteagecaga
                                                                        1200
 cacaggtact gaaatcatgt catctgcggc aacatggtgg aacctaccca atcacacatc
                                                                        1260
 aagagatgaa gacactgcag tatatctgca caacgtaata ctcttcatcc ataacaaaat
                                                                        1320
 aatataattt teetetggag eeatatggat gaactatgaa ggaagaaete eeegaagaag
                                                                        1380
 ccagtcgcag agaagccaca ctgaagctct gtcctcagcc atcagcgcca cggacaggar
                                                                        1440
 tgtgtttctt ccccagtgat gcagcctcaa gttatcccga agctgccgca gcacacggtg
                                                                       1500
 gctcctgaga aacaccccag ctcttccggt ctaacacagg caagtcaata aatgtgataa
                                                                       1560
 tcacataaac agaattaaaa gcaaagtcac ataagcatct caacagacac agaaaaggca
                                                                       1620
 tttgacaaaa tccagcatcc ttgtatttat tgttgcagtt ctcagaggaa atgcttctaa
                                                                       1680
 cttttcccca tttagtatta tgttggctgt gggcttgtca taggtggttt ttattacttt
                                                                       1740
 aaggtatgte eettetatge etgttttget gagggtttta attetegtge e
                                                                       1800
                                                                       1851
       <210> 367
       <211> 668
       <212> DNA
       <213> Homo sapien
       <400> 367
cttgagcttc caaataygga agactggccc ttacacasgt caatgttaaa atgaatgcat
ttcagtattt tgaagataaa attrgtagat ctataccttg ttttttgatt cgatatcagc
                                                                        60
accrtataag agcagtgctt tggccattaa tttatctttc attrtagaca gcrtagtgya
                                                                       120
gagtggtatt tccatactca tctggaatat ttggatcagt gccatgttcc agcaacatta
                                                                       180
acgcacattc atcttcctgg cattgtacgg cctgtcagta ttagacccaa aaacaaatta
                                                                       240
catatcttag gaattcaaaa taacattcca cagctttcac caactagtta tatttaaagg
                                                                       300
agaaaactca tttttatgcc atgtattgaa atcaaaccca cctcatgctg atatagttgg
                                                                       360
ctactgcata cctttatcag agctgtcctc tttttgttgt caaggacatt aagttgacat
                                                                       420
cgtctgtcca gcaggagttt tactacttct gaattcccat tggcagaggc cagatgtaga
                                                                       480
gcagtcctat gagagtgaga agacttttta ggaaattgta gtgcactagc tacagccata
                                                                       540
gcaatgattc atgtaactgc aaacactgaa tagcctgcta ttactctgcc ttcaaaaaaa
                                                                       600
                                                                       660
                                                                       668
```

<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

<400> 368 60 tgggctgggc trgaatcccc tgctggggtt ggcaggtttt ggctgggatt gacttttytc 120 ttcaaacaga ttggaaaccc ggagttacct gctagttggt gaaactggtt ggtagacgcg 180 atctgttggc tactactggc ttctcctggc tgttaaaagc agatggtggt tgaggttgat 240 tccatgccgg ctgcttcttc tgtgaagaag ccatttggtc tcaggagcaa gatgggcaag 300 tggtgctgcc gttgcttccc ctgctgcagg gagagcggca agagcaacgt gggcacttct 360 ggagaccacg acgactetge tatgaagaca etcaggagca agatgggcaa gtggtgeege 420 cactgettee cetgetgeag ggggagtgge aagageaacg tgggegette tggagaceae 480 gacgaytctg ctatgaagac actcaggaac aagatgggca agtggtgctg ccactgcttc 540 ccctgctgca gggggagcrg caagagcaag gtgggcgctt ggggagacta cgatgacagt 600 gccttcatgg agcccaggta ccacgtccgt ggagaagatc tggacaagct ccacagagct 660 gcctggtggg gtaaagtccc cagaaaggat ctcatcgtca tgctcaggga cactgacgtg 720 aacaagaagg acaagcaaaa gaggactgct ctacatctgg cctctgccaa tgggaattca 780 gaagtagtaa aactcstgct ggacagacga tgtcaactta atgtccttga caacaaaaag 840 aggacagete tgayaaagge egtacaatge caggaagatg aatgtgegtt aatgttgetg 900 gaacatggca ctgatccaaa tattccagat gagtatggaa ataccactct rcactaygct 960 rtctayaatg aagataaatt aatggccaaa gcactgctct tatayggtgc tgatatcgaa 1020 tcaaaaaaca aggtatagat ctactaattt tatcttcaaa atactgaaat gcattcattt 1080 taacattgac gtgtgtaagg gccagtcttc cgtatttgga agctcaagca taacttgaat 1140 gaaaatattt tgaaatgacc taattatctm agactttatt ttaaatattg ttatttcaa 1200 agaagcatta gagggtacag ttttttttt ttaaatgcac ttctggtaaa tacttttgtt 1260 gaaaacactg aatttgtaaa aggtaatact tactattttt caatttttcc ctcctaggat 1320 ttttttcccc taatgaatgt aagatggcaa aatttgccct gaaataggtt ttacatgaaa 1380 actccaagaa aagttaaaca tgtttcagtg aatagagatc ctgctccttt ggcaagttcc 1440 taaaaaacag taatagatac gaggtgatgc gcctgtcagt ggcaaggttt aagatatttc 1500 tgatctcgtg cc 1512 <210> 369 <211> 1853 <212> DNA <213> Homo sapien <400> 369 60 tgggctgggc trgaatcccc tgctggggtt ggcaggtttt ggctgggatt gacttttytc 120 ttcaaacaga ttggaaaccc ggagttacct gctagttggt gaaactggtt ggtagacgcg 180 atctgttggc tactactggc ttctcctggc tgttaaaagc agatggtggt tgaggttgat 240 tccatgccgg ctgcttcttc tgtgaagaag ccatttggtc tcaggagcaa gatgggcaag 300 tggtgctgcc gttgcttccc ctgctgcagg gagagcggca agagcaacgt gggcacttct 360 ggagaccacg acgactctgc tatgaagaca ctcaggagca agatgggcaa gtggtgccgc 420 cactgcttcc cctgctgcag ggggagtggc aagagcaacg tgggcgcttc tggagaccac 480 gacgaytctg ctatgaagac actcaggaac aagatgggca agtggtgctg ccactgcttc 540 ccctgctgca gggggagcrg caagagcaag gtgggcgctt ggggagacta cgatgacagy 600 gccttcatgg akcccaggta ccacgtccrt ggagaagatc tggacaagct ccacagagct 660 gcctggtggg gtaaagtccc cagaaaggat ctcatcgtca tgctcaggga cackgaygtg 720 aacaagargg acaagcaaaa gaggactgct ctacatctgg cctctgccaa tgggaattca 780 gaagtagtaa aactcstgct ggacagacga tgtcaactta atgtccttga caacaaaaag 840 aggacagete tgayaaagge egtacaatge caggaagatg aatgtgegtt aatgttgetg 900 gaacatggca ctgatccaaa tattccagat gagtatggaa ataccactct rcactaygct 960 rtctayaatg aagataaatt aatggccaaa gcactgctct tatayggtgc tgatatcgaa 1020 tcaaaaaaca agcatggcct cacaccactg ytacttggtr tacatgagca aaaacagcaa 1080 gtsgtgaaat ttttaatyaa gaaaaaagcg aatttaaaat gcrctggata gatatggaag 1140 ractgetete atacttgetg tatgttgtgg atcageaagt atagteagee ytetaettga 1200 gcaaaatrtt gatgtatett eteaagatet ggaaagaegg eeagagagta tgetgtttet 1260

agtcatcatc atgtaatttg ccagttactt tctgactaca aagaaaaaca gatgttaaaa atctcttctg aaaacagcaa tccagaacaa gacttaaagc tgacatcaga ggaagagtca 1320 caaaggctta aaggaagtga aaacagccag ccagaggcat ggaaactttt aaatttaaac 1380 ttttggttta atgtttttt tttttgcctt aataatatta gatagtccca aatgaaatwa 1440 cctatgagac taggctttga gaatcaatag attcttttt taagaatctt ttggctagga 1500 gcggtgtctc acgcctgtaa ttccagcacc ttgagaggct gaggtgggca gatcacgaga 1560 tcaggagatc gagaccatcc tggctaacac ggtgaaaccc catctctact aaaaatacaa 1620 aaacttagct gggtgtggtg gcgggtgcct gtagtcccag ctactcagga rgctgaggca 1680 ggagaatggc atgaacccgg gaggtggagg ttgcagtgag ccgagatccg ccactacact 1740 1800 1853 <210> 370 <211> 2184 <212> DNA <213> Homo sapien <400> 370 ggcacgagaa ttaaaaccct cagcaaaaca ggcatagaag ggacatacct taaagtaata aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 60 tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 120 tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 180 ttattgactt gcctgtgtta gaccggaaga gctggggtgt ttctcaggag ccaccgtgtg 240 ctgcggcagc ttcgggataa cttgaggctg catcactggg gaagaaacac aytcctgtcc 300 gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 360 ggagttette etteatagtt catecatatg getecagagg aaaattatat tattttgtta 420 tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 480 ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 540 aaagtgtttg tttgtgaatg gatattgtgg tttctggatc tcatcctctg tgggtggaca 600 gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata 660 ccatcgtgca tgcatctttc atttcctgca tttcttcctc cctggatgga cagggggagc 720 ggcaagagca acgrgggcac ttctggagac cacaacgact cctctgtgaa gacgcttggg 780 agcaagaggt gcaagtggtg ctgccactgc ttcccctgct gcaggggagc ggcaagagca 840 acgtggtcgc ttggggagac tacgatgaca gcgccttcat ggatcccagg taccacgtcc 900 atggagaaga tctggacaag ctccacagag ctgcctggtg gggtaaagtc cccagaaagg 960 atctcatcgt catgctcagg gacacggatg tgaacaagag ggacaagcaa aagaggactg 1020 ctctacatct ggcctctgcc aatgggaatt cagaagtagt aaaactcgtg ctggacagac 1080 gatgtcaact taatgtcctt gacaacaaaa agaggacagc tctgacaaag gccgtacaat 1140 gccaggaaga tgaatgtgcg ttaatgttgc tggaacatgg cactgatcca aatattccag 1200 atgagtatgg aaataccact ctacactatg ctgtctacaa tgaagataaa ttaatggcca 1260 aagcactgct cttatacggt gctgatatcg aatcaaaaaa caagcatggc ctcacaccac 1320 tgctacttgg tatacatgag caaaaacagc aagtggtgaa atttttaatc aagaaaaaag 1380 cgaatttaaa tgcgctggat agatatggaa gaactgctct catacttgct gtatgttgtg 1440 gatcagcaag tatagtcagc cctctacttg agcaaaatgt tgatgtatct tctcaagatc 1500 tggaaagacg gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact 1560 ttctgactac aaagaaaaac agatgttaaa aatctcttct gaaaacagca atccagaaca 1620 agacttaaag ctgacatcag aggaagagtc acaaaggctt aaaggaagtg aaaacagcca 1680 gccagaggca tggaaacttt taaatttaaa cttttggttt aatgttttt ttttttgcct 1740 taataatatt agatagtccc aaatgaaatw acctatgaga ctaggctttg agaatcaata 1800 gattetttt ttaagaatet tttggetagg ageggtgtet caegeetgta attecageae 1860 cttgagaggc tgaggtgggc agatcacgag atcaggagat cgagaccatc ctggctaaca 1920 cggtgaaacc ccatctctac taaaaataca aaaacttagc tgggtgtggt ggcgggtgcc 1980 tgtagtccca gctactcagg argctgaggc aggagaatgg catgaacccg ggaggtggag 2040 gttgcagtga gccgagatcc gccactacac tccagcctgg gtgacagagc aagactctgt 2100

Ctcaaaaaa aaaaaaaaa aaaa

```
<210> 371
      <211> 1855
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(1855)
      <223> n = A, T, C \text{ or } G
      <400> 371
tgcacgcatc ggccagtgtc tgtgccacgt acactgacgc cccctgagat gtgcacgccg
                                                                        60
cacgcgcacg ttgcacgcgc ggcagcggct tggctggctt gtaacggctt gcacgcgcac
                                                                       120
geogeeceg cataaccgte agactggeet gtaacggett geaggegeac geogeacgeg
                                                                       180
cgtaacggct tggctgccct gtaacggctt gcacgtgcat gctgcacgcg cgttaacggc
                                                                       240
ttggctggca tgtagccgct tggcttggct ttgcattytt tgctkggctk ggcgttgkty
                                                                       300
tettggattg acgetteete ettggatkga egttteetee ttggatkgae gttteytyty
                                                                       360
tegegtteet tigetggact tgacettity tetgetgggt tiggeattee titggggtgg
                                                                       420
                                                                       480
getgggtgtt tteteegggg gggktkgeee tteetggggt gggegtgggk egeeeceagg
gggcgtgggc tttccccggg tgggtgtggg ttttcctggg gtggggtggg ctgtgctggg
                                                                       540
atcccctgc tggggttggc agggattgac ttttttcttc aaacagattg gaaacccgga
                                                                       600
gtaacntgct agttggtgaa actggttggt agacgcgatc tgctggtact actgtttctc
                                                                       660
ctggctgtta aaagcagatg gtggctgagg ttgattcaat gccggctgct tcttctgtga
                                                                       720
agaagccatt tggtctcagg agcaagatgg gcaagtggtg cgccactgct tcccctgctg
                                                                       780
cagggggagc ggcaagagca acgtgggcac ttctggagac cacaacgact cctctgtgaa
                                                                       840
                                                                       900
gacgettggg ageaagaggt geaagtggtg etgeecaetg etteecetge tgeaggggag
cggcaagagc aacgtggkcg cttggggaga ctacgatgac agcgccttca tggakcccag
                                                                       960
gtaccacgtc crtggagaag atctggacaa gctccacaga gctgcctggt ggggtaaagt
                                                                      1020
ccccagaaag gateteateg teatgeteag ggacaetgay gtgaacaaga rggacaagea
                                                                      1080
aaagaggact gctctacatc tggcctctgc caatgggaat tcagaagtag taaaactcgt
                                                                      1140
gctggacaga cgatgtcaac ttaatgtcct tgacaacaaa aagaggacag ctctgacaaa
                                                                      1200
ggccgtacaa tgccaggaag atgaatgtgc gttaatgttg ctggaacatg gcactgatcc
                                                                      1260
aaatattcca gatgagtatg gaaataccac tctacactat gctgtctaca atgaagataa
                                                                      1320
attaatggcc aaagcactgc tcttatacgg tgctgatatc gaatcaaaaa acaaggtata
                                                                      1380
gatctactaa ttttatcttc aaaatactga aatgcattca ttttaacatt gacgtgtgta
                                                                      1440
agggccagtc ttccgtattt ggaagctcaa gcataacttg aatgaaaata ttttgaaatg
                                                                      1500
acctaattat ctaagacttt attttaaata ttgttatttt caaagaagca ttagagggta
                                                                      1560
                                                                      1620
cagtttttt tttttaaatg cacttctggt aaatactttt gttgaaaaca ctgaatttgt
                                                                      1680
aaaaggtaat acttactatt tttcaatttt tccctcctag gatttttttc ccctaatgaa
                                                                      1740
tqtaaqatqq caaaatttgc cctgaaatag gttttacatg aaaactccaa gaaaagttaa
acatgtttca gtgaatagag atcctgctcc tttggcaagt tcctaaaaaa cagtaataga
                                                                      1800
tacgaggtga tgcgcctgtc agtggcaagg tttaagatat ttctgatctc gtgcc
                                                                      1855
      <210> 372
      <211> 1059
      <212> DNA
      <213> Homo sapien
      <400> 372
gcaacgtggg cacttctgga gaccacaacg actcctctgt gaagacgctt gggagcaaga
                                                                        60
ggtgcaagtg gtgctgccca ctgcttcccc tgctgcaggg gagcggcaag agcaacgtgg
                                                                       120
gegettgrgg agactmegat gacagygeet teatggagee caggtaceae gteegtggag
                                                                       180
aagatctgga caagctccac agagctgccc tggtggggta aagtccccag aaaggatctc
                                                                       240
ategteatge teagggacae tgaygtgaac aagarggaca agcaaaagag gactgeteta
                                                                       300
catctggcct ctgccaatgg gaattcagaa gtagtaaaac tcstgctgga cagacgatgt
                                                                       360
```

```
caacttaatg tccttgacaa caaaaagagg acagctctga yaaaggccgt acaatgccag
  gaagatgaat gtgcgttaat gttgctggaa catggcactg atccaaatat tccagatgag
                                                                         420
  tatggaaata ccactetrea etaygetree tayaatgaag ataaattaat ggecaaagea
                                                                         480
  ctgctcttat ayggtgctga tatcgaatca aaaaacaagg tatagatcta ctaattttat
                                                                         540
  cttcaaaata ctgaaatgca ttcattttaa cattgacgtg tgtaagggcc agtcttccgt
                                                                         600
  atttggaagc tcaagcataa cttgaatgaa aatattttga aatgacctaa ttatctaaga
                                                                         660
  ctttatttta aatattgtta ttttcaaaga agcattagag ggtacagttt tttttttta
                                                                         720
  aatgcacttc tggtaaatac ttttgttgaa aacactgaat ttgtaaaagg taatacttac
                                                                         780
  tatttttcaa tttttccctc ctaggatttt tttcccctaa tgaatgtaag atggcaaaat
                                                                         840
  ttgccctgaa ataggtttta catgaaaact ccaagaaaag ttaaacatgt ttcagtgaat
                                                                         900
  agagatectg eteetttgge aagtteetaa aaaacagtaa tagataegag gtgatgegee
                                                                         960
  tgtcagtggc aaggtttaag atatttctga tctcgtgcc
                                                                        1020
                                                                        1059
        <210> 373
        <211> 1155
        <212> DNA
        <213> Homo sapien
       <400> 373
 atggtggttg aggttgattc catgccggct gcctcttctg tgaagaagcc atttggtctc
 aggagcaaga tgggcaagtg gtgctgccgt tgcttcccct gctgcaggga gagcggcaag
                                                                         60
 agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag
                                                                        120
 atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg
                                                                        180
 ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag
                                                                        240
 tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg
                                                                        300
 ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg
                                                                        360
 gacaagetee acagagetge etggtggggt aaagteeeea gaaaggatet categteatg
                                                                        420
 ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc
                                                                        480
 totgocaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat
                                                                        54 C
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa
                                                                        600
tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat
                                                                        660
accactetge actaegetat etataatgaa gataaattaa tggeeaaage actgetetta
                                                                        720
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta
                                                                        780
catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca
                                                                        840
ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata
                                                                        900
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg
                                                                        960
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac
                                                                      1020
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaaa tgtctcaaga
                                                                      1080
                                                                      1140
accagaaata aataa
                                                                      1155
      <210> 374
      <211> 2000
      <212> DNA
      <213> Homo sapien
      <400> 374
atggtggttg aggttgattc catgccggct gcctcttctg tgaagaagcc atttggtctc
aggagcaaga tgggcaagtg gtgctgccgt tgcttcccct gctgcaggga gagcggcaag
                                                                        60
agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag
                                                                       120
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg
                                                                       180
ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag
                                                                       240
tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg
                                                                       300
ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg
                                                                       360
gacaagetee acagagetge etggtggggt aaagteeeca gaaaggatet categteatg
                                                                       420
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc
                                                                       480
                                                                      540
```

tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcca	ggaagatgaa	660
tgtgcgttaa	tgttgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactgtt	acttggtgta	840
catgagcaaa	aacagcaagt	cgtgaaattt	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgctgtat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaag	1140
ctgacatcag	aggaagagtc	acaaaggttc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	aggttgaaga	agaaatgaag	1260
aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaatggtgt	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaagg	aagagcagaa	cacctgaaaa	tcagcaattt	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atttgcgaat	tagtttctga	ctacaaagaa	1440
aaacagatgc	caaaatactc	ttctgaaaac	agcaacccag	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaag	gcttgagggc	agtgaaaatg	gccagccaga	gctagaaaat	1560
tttatggcta	tcgaagaaat	gaagaagcac	ggaagtactc	atgtcggatt	cccagaaaac	1620
ctgactaatg	gtgccactgc	tggcaatggt	gatgatggat	taattcctcc	aaggaagagc	1680
agaacacctg	aaagccagca	atttcctgac	actgagaatg	aagagtatca	cagtgacgaa	1740
caaaatgata	ctcagaagca	attttgtgaa	gaacagaaca	ctggaatatt	acacgatgag	1800
attctgattc	atgaagaaaa	gcagatagaa	gtggttgaaa	aaatgaattc	tgagctttct	1860
cttagttgta	agaaagaaaa	agacatcttg	catgaaaata	gtacgttgcg	ggaagaaatt	1920
gccatgctaa	gactggagct	agacacaatg	aaacatcaga	gccagctaaa	aaaaaaaaa	1980
aaaaaaaaa	aaaaaaaaa					2000

<210> 375

<211> 2040

<212> DNA

<213> Homo sapien

<400> 375

atggtggttg aggttgattc catgccggct gcctcttctg tgaagaagcc atttggtctc 60 aggagcaaga tgggcaagtg gtgctgccgt tgcttcccct gctgcaggga gagcggcaag 120 agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180 atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg 240 ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag 300 tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg 360 ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg 420 gacaagetee acagagetge etggtggggt aaagteecea gaaaggatet categteatg 480 540 ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat 600 gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa 660 tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat 720 accactetge actacgetat etataatgaa gataaattaa tggeeaaage actgetetta 780 840 tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca 900 ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata 960 gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg 1020 gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac 1080 aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaca agacttaaag 1140 1200 ctgacatcag aggaagagtc acaaaggttc aaaggcagtg aaaatagcca gccagagaaa atgtctcaag aaccagaaat aaataaggat ggtgatagag aggttgaaga agaaatgaag 1260 aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc 1320 aatggtgata atggattaat tootcaaagg aagagcagaa cacotgaaaa toagcaattt 1380

cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gaaaagatct 1500 caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa 1560 gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc 1620 actgctggca atggtgatga tggattaatt cctccaagga agagcagaac acctgaaagc 1680 cagcaatttc ctgacactga gaatgaagag tatcacagtg acgaacaaaa tgatactcag 1740 aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1800 gaaaagcaga tagaagtggt tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa 1860 gaaaaagaca tettgeatga aaatagtaeg ttgegggaag aaattgeeat getaagaetg 1920 1980 2040

<210> 376

WO 00/04149

<211> 329

<212> PRT

<213> Homo sapien

<400> 376

Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu 25 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val 75 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val 85 90 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr 105 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp 120 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp 135 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser 150 155 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Cys 165 170 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala 180 185 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr 215 220 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Tyr 230 235 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu 250 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys 260 265 270 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu 280 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu

```
300
                       295
    290
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
             310
                                       315
Ser Met Leu Phe Leu Val Ile Ile Met
               325
      <210> 377
      <211> 148
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(148)
      <223> Xaa = Any Amino Acid
      <400> 377
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
                                    10
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
                               25
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
                    70
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
                                   90
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
                               105
            100
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
                          120
Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser
    130
                        135
Lys Asn Lys Val
145
      <210> 378
      <211> 1719
      <212> PRT
      <213> Homo sapien
      <400> 378
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
                                25
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
                            40
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
```

				85					90					95	
			ΤC	10				10	s Ph 5	e Pr			7 7	g GI	y Ser
							12	p Gl	y As			1 2	p Se	r Al	a Phe
	10	U				135	l Arq	g Gl			141	u As	p Ly		u His
173	•				150	,				15	s Ası	o Le			l Met
				T 6:	>				170	p Ly:	s Glr			17	160 r Ala
			т 9	U				189	5				10	s Le	u Leu
		13	-				200)				201	s Ly:	s Ar	g Thr
	210	•				215)				220	ı Cys	s Ala		u Met
223					230					235	Asp	Glu			y Asn 240
				245	1				250)				25	a Lys
			200	,				265					270	His	s Gly
		2/:	•				280					285	Glr	ı Val	l Val
	230					295					300				y Tyr
303					310					315					Tle 320
				325					330					225	Leu
			340					345					3 5 0		
		222		Leu			360					365			
	3/0			Ser		375					300				
303				Met	390					395					400
				Pro 405					410					11E	
			420	Pro				425					420		
		433		His			440					445			
	- 30			Cys		455					460				
403				Gly	4/0					475					400
				Lys 485					490					4 Q E	
Cys i			500					505					E 1 0		
Asp S	JEI	515	rne	Met	GIU	Pro .	Arg 520	Tyr	His	Val	Arg	Gly 525	Glu	Asp	Leu

As	-	ys 30	Leu	His	Arg	Ala	Ala 535	Trp	Trp	Gly	Lys	Val 540	Pro	Arg	Lys	Asp
Le 54		le	Val	Met	Leu	Arg 550	Asp	Thr	Asp	Val	Asn 555	Lys	Lys	Asp	Lys	Gln 560
Ly	s A	rg	Thr	Ala	Leu 565	His	Leu	Ala	Ser	Ala 570	Asn	Gly	Asn	Ser	Glu 575	Val
Va	1 L	ys	Leu	Leu 580	Leu	Asp	Arg	Arg	Cys 585	Gln	Leu	Asn	Val	Leu 590	Asp	Asn
Ly	s L	ys	Arg 595	Thr	Ala	Leu	Ile	Lys 600	Ala	Val	Gln	Cys	Gln 605	Glu	Asp	Glu
Су		la 10	Leu	Met	Leu	Leu	Glu 615	His	Gly	Thr	Asp	Pro 620	Asn	Ile	Pro	Asp
62	:5	_		Asn		630					635					640
				Lys	645					650					655	
		_		Gly 660					665					670		
			675	Val				680					685			
	6	90	_	Tyr			695					700				
70)5			Ile		710					715					720
				Leu	725					730					735	
				Val 740		-			745					750		
			755	Ile				760					765			
	7	770		Glu			775					780				
78	35			Lys		790					795					800
	_			Glu	805					810					815	
				Asn 820					825					830		
			835	Pro				840					845			
	8	350		Glu			855					860				
86	55	_		Glu		870					875					880
				Asp	885					890					895	
				Glu 900		•			905					910		
			915	Lys				920					925			
	9	930		Gly			935					940				
9	45	_	_	Ser		950					955					960
A	sn (Glu	Glu	Tyr	His	Ser	Asp	Glu	GIn	Asn	Asp	Thr	GIN	ьys	GIN	ьue

				96	5										
Cys	G1	u Gl	u Gl			. 613	. T3.	. T.o.	97	0	. ~.		e Leu	97	5
			20	0				00	_						
			_				1 (1)	111				1 ^	990 r Glu		
Leu	Se:	r Cy 10	s Ly	s Ly	s Glu	Lys 101	a Asp) Ile	e Le	u Hi	s Glu	ı Ası	us n Ser	Th	r Le
Arg	Glu		u Ile	e Ala	a Met	Leu	ı Arg	J Lei	ı Gl	u Lei	102 Asp	20 > Th:	r Met	Lv	s Hi
	_				T 0 3	U				10.	2 =				
				T ()	: 0				יחו	50			l Asp		
			T (, ,				106	. 5				g Ser	Lys	s M∈
Gly	Lys	Tr	o Cys 75	суя	Arg	Cys	Phe	Pro	Cys	в Суз	Arg		107 Ser	Gl _}	r Ly
Ser	Asn	Va:	l Gly	/ Thr	Ser	Gly	Asp	His	Asp) Asp	Ser	108 Ala	Met	Lys	Th
Leu			Lvs	: Met	Glv	109		C	3	. •••	110	0			
	-									777	_		Pro		
					ິ				717	חו			His		_
			T T Z	v				774	5				Cys	Cys	Hi
			_				1161	3				776	Gly	Ala	
Gly	Asp 117	Tyr 0	Asp	Asp	Ser	Ala 1175	Phe	Met	Glu	Pro			His	Val	Arg
Gly	Glu	Asp	Leu	Asp	Lys	Leu	His	Arq	Ala	Ala	1180	ט יייט	Gly	Lvc	170
					エエコロ	1				110					
				120)				121	Ω			Val	2 2 2 1	Lys
			124	U				1775	His	Leu			Ala 1230	Asn	Gly
Asn	Ser	Glu 123	Val	Val	Lys	Leu	Leu 1240	Leu	Asp	Arg	Arg		Gln	Leu	Asr
Val :	Leu 1250	Asp		Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	1245 Ala	Val	Gln	Cys
	4450	•				エとうう)				1260	١			
					12/0					7775			Thr .		
				1400)				1290	1			Ala		Tyr
Asn (3lu	Asp	Lys 1300	Leu)	Met 1	Ala	Lys .	Ala 1305	Leu	Leu	Leu	Tyr	Gly A	Ala	Asp
Ile (Glu	Ser 1315	Lys		Lys I	His	Gly :	Leu	Thr	Pro			1310 Leu (Sly	Val
His (3lu	Gln		Gln	Gln V	/al '	1320 Val :	Lys	Phe	Leu	Ile	1325 Lys	Lys I	bys	Ala
Asn I	-330					レメスシ					1340		- Ile I		
-515					T350					1355					
				TOOD					1 770				Glu G	200	
			T200				1	1385					Arg G	lu '	
Ala V	al :	Ser 1395			His H	lis V	Jal 1	[le (Cvs	Gln ·	Leu I	.e	1390 Ser A	an '	Th exc

Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu 1415 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly 1430 1435 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn 1450 1445 1455 Lys Asp Gly Asp Arg Glu Val Glu Glu Met Lys Lys His Glu Ser 1460 1465 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly 1485 1480 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu 1500 1495 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys 1510 1515 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser 1530 1525 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu 1540 1545 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser 1560 1565 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe **157**5 1580 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe 1590 1595 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly 1610 1605 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro 1625 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln 1640 1645 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile 1655 1660 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser 1675 1670 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn 1690 1685 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr 1700 1705 Met Lys His Gln Ser Gln Leu 1715

<210> 379

<211> 656

<212> PRT

<213> Homo sapien

<400> 379

 Met
 Val
 Val
 Glu
 Val
 Asp
 Ser
 Met
 Pro
 Ala
 Ala
 Ser
 Ser
 Val
 Lys
 Lys
 Lys
 Ala
 Ala
 Ser
 Ser
 Val
 Lys
 Lys
 Lys
 Lys
 Trp
 Cys
 Cys
 Cys
 Cys
 Phe

 Pro
 Cys
 Cys
 Arg
 Glu
 Ser
 Gly
 Lys
 Ser
 Asn
 Val
 Gly
 Cys
 Arg
 Cys
 Phe

 35
 40
 40
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45
 45<

0.5					70					75					sn Val
				85					90	a Me	t Ly			0.5	g Asn
			101	U				10	s Ph	e Pr			7 7	g Gl	y Ser
		<u> </u>	9				120)				12	p Se	r Al	a Phe
	10	•				13:	l Arg	g Gly			2/1	ı As	p Ly		u His
443					120	,				15	s Asp	Le			1 Met 160
				703)				170	Lys	s Glr			17	r Ala
			100	,				185	5				104	s Le	u Leu
		エフこ	,				200	}				205	Lys	s Ar	g Thr
	210	,				215)				220	r			u Met
227					230					235					Asn 240
				240					250	1				0.55	240 a Lys
			200					265					270	1	Gly
		2/5					280					285			Val
	230					295					300				Tyr
303					3 T U					315					Ile 320
				325					330					335	Leu
			Thr 340					345					350		
		222	Leu				360					365			
	3,0					375					380				Glu
303			Gln		390					395					400
			Glu	405					410					415	
			Lys 420					425					430		
		433	Gly				440					445			
	450		Ser			455					460				
Ser 465					4/0					475					400
Lys				485					490					495	
Leu :	ьys	⊥eu	ınr	ser (GIU (GIu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu

	500			505		510	
Asn Gly	Gln Pro 515	Glu Leu	Glu Asn 520		Ala Ile	Glu Glu 525	Met Lys
Lys His 530	Gly Ser	Thr His	Val Gly 535		Glu Asn 540	Leu Thr	Asn Gly
Ala Thr 545	Ala Gly	Asn Gly 550	_	Gly Leu	Ile Pro 555	Pro Arg	Lys Ser 560
Arg Thr	Pro Glu	Ser Gln 565	Gln Phe	Pro Asp 570		Asn Glu	Glu Tyr 575
His Ser	Asp Glu 580		Asp Thr	Gln Lys 585	Gln Phe	Cys Glu 590	Glu Gln
Asn Thr	Gly Ile 595	Leu His	Asp Glu 600	Ile Leu	Ile His	Glu Glu 605	Lys Gln
Ile Glu 610	Val Val	Glu Lys	Met Asn 615	Ser Glu	Leu Ser 620	Leu Ser	Cys Lys
Lys Glu 625	Lys Asp	Ile Leu 630		Asn Ser	Thr Leu 635	Arg Glu	Glu Ile 640
Ala Met	Leu Arg	Leu Glu 645	Leu Asp	Thr Met 650	Lys His	Gln Ser	Gln Leu 655

<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe 25 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp 40 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp 55 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val 70 75 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser 105 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe 120 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His 140 135 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met 150 155 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala 165 170 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu 180 185 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met 215 220 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn

225 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Me 245 250 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Ly 260 265 27 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gl 275 280 285 Lys Phe Leu Ile Lys Lys Ala Asn Leu Asn Ala Leu As 290 295 300 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Al 305 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gl: 325 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His 340 345 356 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr 370 375 Leu Tyr Ala Val Leu Lys Leu Thr 376	et Ala Lys 255 s His Gly 0 n Val Val p Arg Tyr a Ser Ile 320 n Asp Leu	Gly Val Tyr
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Ly 260 265 27 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gl 275 280 285 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu As 290 295 300 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Al 305 310 315 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gl: 325 330 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His 340 345 355 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu 355 360 365 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr 370 375	255 s His Gly 0 n Val Val p Arg Tyr a Ser Ile 320 n Asp Leu	Gly Val Tyr
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gl 275	s His Gly 0 n Val Val p Arg Tyr a Ser Ile 320 n Asp Leu	Gly Val Tyr
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gl 275	n Val Val p Arg Tyr a Ser Ile 320 n Asp Leu	Tyr
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu As 290 295 300 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Al 305 310 315 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gl: 325 330 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His Hi: 340 345 355 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu 355 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thm 370 375	a Ser Ile 320 n Asp Leu	
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Al 305 310 315 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gl: 325 330 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His Hi: 340 345 355 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu 355 360 365 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Th: 370 375	320 n Asp Leu	T10
Val Ser Leu Leu Glu Gln Asn Ile Asp Val Ser Gl Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His Hi	n Asp Leu	320
340 345 350 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu 355 360 365 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thi	335	Leu
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu 355 360 365 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr 370 375 380	s His Val	
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Th 370 380	u Lys Ile	
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro 385 390 395	400	400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu 405 410	ı Val Glu	Glu
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu 420 425 430	ı Glu Asn	
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu 435 440 445		
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp 450 455 460		
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr 465 470 475	400	100
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu 485 490	Gln Asp	Asp
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly 500 505 510		
Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn 515 520 525		
Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met 530 535 540		
His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn 545 550 555		
Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys 565 570		Arg
Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu 580 585 590	575 Tyr His	His
Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu 595 600 605	Gln Asn	Asn
Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys 610 615 620	Gln Ile	lle
Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys 625 630 635		
Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu 645 650	640	Ala
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln 660 665 670	655	

120

180

240 251

```
<210> 381
       <211> 251
       <212> DNA
       <213> Homo sapien
       <400> 381
qqaqaaqcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa
ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg
ccaatatccc aggagaagca ttgggggagtt gggggcaggt gaaggaccca ggactcacac
atcctgggcc tccaaggcag aggagaggt cctcaagaag gtcaggagga aaatccgtaa
caagcagtca g
<210> 382
<211> 3279
<212> DNA
<213> Homo sapiens
<400> 382
cttcctgcag cccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
cactgggagg ggacatcctg cagaaggtag gagtgagcaa acacccgctg caggggaggg 180
gagagecetg eggeaeetgg gggageagag ggageageae etgeeeagge etgggaggag 240
gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagtgag ggatcagggg 300
cagggegega gatggeetea cacagggaag agagggeece teetgeaggg ceteacetgg 360
gccacaggag gacactgctt ttcctctgag gagtcaggag ctgtygatgg tgctggacag 420
aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
qactqcagqq agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
gtggctccag gccttgcccc tgcctgggcc ctcacccagc ctccctcaca gtctcctggc 600
cctcagtctc tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660
gaactgacca tacccagece tgeecaegge cetecatgge teeceaatge cetggagagg 720
ggacatctag tcagagagta gtcctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
gcatcctgca gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840
ggaccttgcc ccttgtgcag gagctggacc ctgaagtccc ctccccatag gccaagactg 900
gageettgtt cectetgttg gaeteeetge ceatattett gtgggagtgg gttetggaga 960
cattrctgtc tgttcctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020
agagatggag ttgcctaggc agttattggg gccaatcttt ctcactgtgt ctctcctcct 1080
ttaccettag ggtgattetg ggggteeact tgtetgtaat ggtgtgette aaggtateae 1140
atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200
gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260
cccctacctc tagtaaattt aagtccacct cacgttctgg catcacttgg cctttctgga 1320
tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gagtcctact 1380
gacctgtgct ttctggtgtg gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440
tgtatgccaa tgtttctgaa atgggtataa tttcgtcctc tccttcggaa cactggctgt 1500
ctctgaagac ttctcgctca gtttcagtga ggacacacac aaagacgtgg gtgaccatgt 1560
tgtttgtggg gtgcagagat gggaggggtg gggcccaccc tggaagagtg gacagtgaca 1620
caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680
acacacagca aggttgacgc tgtaaacata gcccacgctg tcctgggggc actgggaagc 1740
ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttgttg aaggagggac 1800
tagggggaga aactgaaagc tgattaatta caggaggttt gttcaggtcc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgatc cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
```

WO 00/04149 PCT/US99/15838

gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220 caaggatgta tgataatatg tacaaagtaa ttccaactga ggaagctcac ctgatcctta 2280 gtgtccaggg tttttactgg gggtctgtag gacgagtatg gagtacttga ataattgacc 2340 tgaagtcctc agacctgagg ttcccctagag ttcaaacaga tacagcatgg tccagagtcc 2400 cagatgtaca aaaacaggga ttcatcacaa atcccatctt tagcatgaag ggtctggcat 2460 ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgtc 2520 atctcccagg agttattcaa gggtgagccc tttacttggg atgtacaggc tttgagcagt 2580 gcagggctgc tgagtcaacc ttttattgta caggggatga gggaaaggga gaggatgagg 2640 aagccccct ggggatttgg tttggtcttg tgatcaggtg gtctatgggg ctatccctac 2700 aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760 atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820 gttatgaaga tggttgaaca ccccacacat agcaccggag atatgagatc aacagtttct 2880 tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940 ggggatgcgc tcgggattgg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000 acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060 gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120 cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180 ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240 gttttcagac cttaaaaaaa aaaaaaaaa aaaagtttt 3279

<210> 383

<211> 155

<212> PRT

<213> Homo sapiens

<400> 383

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr 5 10 15

Gly Lys Arg Gly Pro Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
20 25 30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
35 40 45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe 50 55 60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly 65 70 75 80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala 85 90 95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu 100 105 110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
115 120 125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn 130 135 140

Ala Leu Glu Arg Gly His Leu Val Arg Glu 145 150

```
<210> 384
<211> 557
<212> DNA
<213> Homo sapiens
<400> 384
ggatecteta gageggeege etaetaetae taaattegeg geegegtega egaagaagag 60
aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
totgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctqtaqaq agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tececaaqae acateetaaa aggtgttgta atggtgaaaa egtetteett etttattgee 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tctttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaa aaaaaaa
<210> 385
<211> 337
<212> DNA
<213> Homo sapiens
<400> 385
ttcccaggtg atgtgcgagg gaagacacat ttactatect tgatgggget gatteettta 60
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
teteaaagee atetgetgte ttegagtaeg gacacateat caeteetgea ttgttgatea 180
aaacqtqqaq gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc ttttccacat cccggca
<210> 386
<211> 300
<212> DNA
<213> Homo sapiens
<400> 386
gggcccgcta ccggcccagg ccccgcctcg cgagtcctcc tccccgggtg cctgcccgca 60
gcccgctcgg cccagagggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcgc 180
geggaettig ceeggigtgi ggggeggage ggaetgegtg teegeggaeg ggeagegaag 240
atgttageet tegetgeeag gacegtggae egateeeagg getgtggtgt aaceteagee 300
<210> 387
<211> 537
<212> DNA
<213> Homo sapiens
<400> 387
gggccgagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggcttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagaggca ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
```

WO 00/04149 PCT/US99/15838

```
geggeecage actteeteag acacaactte tteetgetge teeagtegtg gggateatea 360
 cttacccacc ccccaagttc aagaccaaat cttccagctg cccccttcgt gtttccctgt 420
 gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
 ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaaa
 <210> 388
 <211> 520
 <212> DNA
 <213> Homo sapiens
 <400> 388
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggttaaa ccagtttgca ttcccctaat gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
ggacccctc cccaacatgc cccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatggtta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tggtgggttt tttttctggt
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens
<400> 389
cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctccccc 120
aacgactttc caaataatct caccagegee ttecagetea ggegteetag aagegtettg 180
aagcotatgg ccagetgtot ttgtgttooc totcaccego ctgtcotcac agctgagact 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag
                                                                   365
<210> 390
<211> 221
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(221)
<223> n = A,T,C or G
<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a
                                                                  221
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A, T, C or G
<400> 391
tqqaqcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcqcqcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
taqccaqqqc actqctqcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagaceteeg getactaeta tgace
                                                                325
<210> 392
<211> 277
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(277)
<223> n = A,T,C or G
<400> 392
atattqttta acteetteet ttatatettt taacatttte atggngaaag gtteacatet 60
agteteactt nggenagngn etectaettg agtetettee eeggeetgnn eeagtngnaa 120
antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccetgtee actaegtgat getgtaggat taaagtetea cagtgggegg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa
                                                                277
<210> 393
<211> 566
<212> DNA
<213> Homo sapiens
<400> 393
actagtccag tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
qaqaaqqtct aqtttqtcca tcaqcattat catqatatca gqactgqtta cttggttaaq 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
cattetetge etgagtttta atttttgtee aaagttattt taatetatae aattaaaage 540
ttttgcctat caaaaaaaa aaaaaa
                                                                566
<210> 394
<211> 384
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
```

```
<222> (1)...(384)
 <223> n = A,T,C or G
 <400> 394
 gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
 tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
 gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
 tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg agcatgacgt 240
 gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
 agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
 tgagcagatg gtttctgagg acgt
 <210> 395
 <211> 399
 <212> DNA
 <213> Homo sapiens
 <400> 395
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttetet ttggaaagee tgggeatete eteactacag acetetgace atgggaeggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac
                                                                   399
<210> 396
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(403)
<223> n = A,T,C or G
<400> 396
tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttetgete cagetgetga taaaacaaat catgtgttta gettgactee 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt
<210> 397
<211> 100
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(100)
<223> n = A,T,C or G
```

```
<400> 397
actagtncag tgtggtggaa ttcgcggccg cgtcgaccta naanccatct ctatagcaaa 60
tccatccccg ctcctggttg gtnacagaat gactgacaaa
<210> 398
<211> 278
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(278)
<223> n = A,T,C or G
<400> 398
geggeeget egacageagt teegeeageg etegeeeetg ggtggggatg tgetgeaege 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg
<210> 399
<211> 298
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(298)
<223> n = A,T,C or G
<400> 399
acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
ggggtgccng catggagcgc atgggcgcg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg
<210> 400
<211> 548
<212> DNA
<213> Homo sapiens
<400> 400
acateaacta ettecteatt ttaaggtatg geagtteect teateceett tteetgeett 60
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatcccg 300
tatacectet caccatecce ttgtetacte tgatgeecce aagatgeaae tgggeageta 360
gttggcccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggccccc ctcctgggat caagcccctc ccaggccctg 480
tecceagese etectgeese ageseacesg ettgeettgg tgeteagese teccattggg 540
                                                                548
agcaggtt
```

WO 00/04149 PCT/US99/15838

```
<210> 401
 <211> 355
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(355)
 <223> n = A,T,C or G
 <400> 401
 actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
 tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
 taagagtggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
 tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc
 <210> 402
 <211> 407
 <212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G
<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G
<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcaccaaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tottaacaac gaccgaaacc cattatttac ataaacctcc attoggtaac catgttgaaa 300
gga
                                                                   303
```

```
<210> 404
<211> 225
<212> DNA
<213> Homo sapiens
<400> 404
aagtqtaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120
acattttcca ctcgtgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat
                                                                   225
<210> 405
<211> 334
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(334)
<223> n = A, T, C or G
<400> 405
gagetgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctcccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
teatececat cecatgeeaa aggaagaeee teeeteettg geteacagee ttetetagge 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactetecae teteteanng tggateceae cect
                                                                   334
<210> 406
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G
<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcaccettg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant
                                                                   216
<210> 407
<211> 413
<212> DNA
<213> Homo sapiens
<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
```

```
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
 tgccagacag gagaaagtet teecatgtta aaagacattt attatettgt ttteetgtea 360
 tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag
 <210> 408
 <211> 183
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(183)
 \langle 223 \rangle n = A,T,C or G
 <400> 408
 ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
 tnottaacta gttaatoott aaagggotan ntaatootta actagtooot coattgtgag 120
cattateett ecagtatten cettetnttt tatttaetee tteetggeta eccatgtaet 180
 ntt
                                                                     183
 <210> 409
 <211> 250
 <212> DNA
 <213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C \text{ or } G
<400> 409
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gcccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggccntatgc
                                                                    250
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtettgeaa teccatttge aggateegte tgtgeacatg cetetgtaga gageageatt 120
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atcttttta aactggaaag ttcaattgng aaaatgaata 300
tentge
```

```
<210> 411
<211> 261
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(261)
<223> n = A, T, C or G
<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggngaggcaa a
<210> 412
<211> 241
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(241)
<223> n = A, T, C \text{ or } G
<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
                                                                    241
<210> 413
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A, T, C or G
<400> 413
aactettaca atecaagtga eteatetgtg tgettgaate etttecaetg teteatetee 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t
<210> 414
<211> 234
<212> DNA
<213> Homo sapiens
```

```
<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca
<210> 415
<211> 217
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A,T,C or G
<400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc
                                                                   217
<210> 416
<211> 213
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G
<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag
<210> 417
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G
<400> 417
nagtetteag geceateagg gaagtteaca etggagagaa gteatacata tgtaetgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt
                                                                   303
```

```
<210> 418
<211> 328
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(328)
<223> n = A,T,C or G
<400> 418
tttttggcgg tggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
qcctcaqcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
teagnggtea ggetggtete aaacteetga eeteaagtga tetgeecace teageeteee 300
aaagtgctan gattacaggc cgtgagcc
<210> 419
<211> 389
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G
<400> 419
cctcctcaaq acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
accectgage catggactgg agectgaaag geagegtaca ceetgeteet gatettgetg 120
cttgtttcct ctctgtggct ccattcatag cacagttgtt gcactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
coggetete agecaceaac etcacteget coegeaaatg geacateagt tettetacee 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg
<210> 420
<211> 408
<212> DNA
<213> Homo sapiens
<400> 420
qttcctccta actcctqcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
qtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaageacag 360
acgttgaccg gactttgatg aagtgctatg acaaacctgg caagcccg
                                                                   408
<210> 421
<211> 352
<212> DNA
```

```
<213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(352)
 <223> n = A,T,C or G
 <400> 421
 gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
 gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
 ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgcagtc 180
 ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
 ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
 cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg
 <210> 422
 <211> 337
 <212> DNA
<213> Homo sapiens
<400> 422
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcgg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta
                                                                   310
<210> 424
<211> 370
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A, T, C or G
```

```
<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
qqaqaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtettt tttgggteet tetteteeac cacgatatae ttgcagteet 180
ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C \text{ or } G
<400> 425
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattateca ttatnttaag ggttgaette aggntacage acacagaeaa acatgeecag 180
gaggntntca ggaccgctcg atgtnttntg aggagg
                                                                 216
<210> 426
<211> 596
<212> DNA
<213> Homo sapiens
<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct
<210> 427
<211> 107
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A, T, C or G
<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
```

```
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng
                                                                    107
 <210> 428
 <211> 38
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(38)
 <223> n = A,T,C or G
 <400> 428
gaacttccna anaangactt tattcactat tttacatt
                                                                    38
 <210> 429
 <211> 544
 <212> DNA
<213> Homo sapiens
<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagage ggetgeagee etgeggttea gattaaaate egagaattgt atagaegeeg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
geetteeact teagttacae eteacteace atceteteet gttggttetg tgetgettea 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat
<210> 430
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (507)
<223> n = A,T,C or G
<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
catteteete tggeetetaa tagteaatga ttgtgtagee atgeetatea gtaaaaagat 480
ttttgagcaa aaaaaaaa aaaaaaa
<210> 431
<211> 392
```

```
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A, T, C or G
<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaaqaaa qcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatqqct aaatqtqaga ttagcacaqc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaaqtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
                                                                    392
<210> 432
<211> 387
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A, T, C \text{ or } G
<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
nqtaqtccaa gctctcggna gtccagccac tgngaaacat gctcccttta gattaacctc 180
qtqqacnctn ttqttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attetqttqc ttetggggca ttteettgng atgeagagga ceaceacaca gatgacagea 300
atctqaattq ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt
<210> 433
<211> 281
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(281)
<223> n = A, T, C or G
<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggenetat ttgggttgge tggaggaget gtggaaaaca tggagagatt ggegetggag 180
ategeogtgg ctattecten ttgntattae accagngagg ntetetgtnt geceactggt 240
                                                                    281
tnnaaaaccg ntatacaata atgatagaat aggacacaca t
<210> 434
<211> 484
```

```
<212> DNA
 <213> Homo sapiens
 <400> 434
 ttttaaaata agcatttagt gctcagtccc tactgagtac tctttctctc ccctcctctg 60
 aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta
<210> 435
<211> 424
<212> DNA
<213> Homo sapiens
<400> 435
gcgccgctca gagcaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagettt caatategea ggttettaet eetetgeete tataagetea aacceaceaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggagggg caagatagat gaggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggcct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac
                                                                   424
<210> 436
<211> 667
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(667)
<223> n = A, T, C or G
<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagtteetga aaggeaggta tageaactga tetteagaaa gaggaactgt gtgeaeeggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gatteettta tggggteagt gggaaaggtg teaatgggae tteggtetee atgeegaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag
                                                                  667
<210> 437
<211> 693
```

```
<212> DNA
<213> Homo sapiens
<400> 437
ctacqtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
ataaaagata attettagee catgttette teeagageag acetgaaatg acageacage 240
aggtactect etatttteac ecetettget tetactetet ggeagteaga eetgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tectatttet aggeactgag ggetgtgggg tacettgtgg tgecaaaaca gateetgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc
                                                                   693
<210> 438
<211> 360
<212> DNA
<213> Homo sapiens
<400> 438
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggtgg agaagaagga cccaaaaaaag acctgttctg tcagtgaatg 240
gataatetaa tgtgetteta gtaggeacag ggeteecagg ecaggeetea tteteetetg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
<210> 439
<211> 431
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A,T,C or G
<400> 439
gttcctnnta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t
                                                                   431
<210> 440
<211> 523
<212> DNA
<213> Homo sapiens
```

```
<400> 440
 agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
 cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
 actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
 taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
 acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
 tatatatatc atagcaaata agtcatctga tgagaacaag cta
                                                                    523
 <210> 441
 <211> 430
 <212> DNA
 <213> Homo sapiens
 <400> 441
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca ccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaageacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag
<210> 442
<211> 362
<212> DNA
<213> Homo sapiens
<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtggggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc
                                                                   362
<210> 443
<211> 624
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G
<400> 443
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgettatt ttaaaagaaa tgtaaagage agaaageaat teaggetace etgeettttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
```

```
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca teettattat taaagteaac getaaaatga atgtgtgtge atatgetaat 480
aqtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G
<400> 444
qcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagetttgt ccaggeetgt gtgtgaacce aatgttttge ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
qctqtqctqq gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cototqcaat otgocaccto otgotggcag gatttgtttt tgcatcotgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
                                                                    425
qtaqa
<210> 445
<211> 414
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(414)
<223> n = A, T, C \text{ or } G
<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcatgtggc agattattgg atgtagtttc ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatqaaaaat tqtqtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag
<210> 446
<211> 631
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(631)
```

```
<223> n = A, T, C \text{ or } G
 <400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g
<210> 447
<211> 585
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G
<400> 447
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agtteetgaa aggeaggtat ageaactgat etteagaaag aggaactgtg tgeaceggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attectttat ggggteagtg ggaaaggtgt caatgggact teggteteea tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta
                                                                   585
<210> 448
<211> 93
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(93)
<223> n = A,T,C or G
<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag
                                                                   93
<210> 449
<211> 706
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(706)
<223> n = A, T, C or G
<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacage atcctgcaga tggtcgggcg cgtcccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcnccca 660
706
<210> 450
<211> 493
<212> DNA
<213> Homo sapiens
<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtgag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagetttac aaacteecat tgeegagggt egaegeggee 480
gcgaatttag tag
<210> 451
<211> 501
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G
<400> 451
gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
geggeegeet aetactaeta aattegegge egegtegaeg tgggateene aetgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactcca 480
```

WO 00/04149 PCT/US99/15838 162

```
tcttaaaaaa aaaaaaaaa a
                                                                    501
 <210> 452
 <211> 51
 <212> DNA
 <213> Homo sapiens
 <220>
<221> misc_feature
 <222> (1)...(51)
 <223> n = A,T,C or G
<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c
                                                                    51
<210> 453
<211> 317
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G
<400> 453
tacatettge tttttcccca ttggaactag tcattaacce atetetgaac tggtagaaaa 60
acatetgaag agetagteta teageatetg geaagtgaat tggatggtte teagaaceat 120
ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc tttatta
<210> 454
<211> 231
<212> DNA
<213> Homo sapiens
<400> 454
ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t
<210> 455
<211> 231
<212> DNA
<213> Homo sapiens
<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggctcc tttctcctct a
```

```
<210> 456
<211> 231
<212> DNA
<213> Homo sapiens
<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcgtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120
tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180
cctttttatt tggtgcagct gctagtcagt ccctgactga cattgccaag t
<210> 457
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (231)
<223> n = A,T,C or G
<400> 457
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g
                                                                   231
<210> 458
<211> 231
<212> DNA
<213> Homo sapiens
<400> 458
aggtetggtt ccccccactt ccactcccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t
<210> 459
<211> 231
<212> DNA
<213> Homo sapiens
<400> 459
ggtaccgagg ctcgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
geoetgeact gttttecete caccacagee atcetgtece teattggete tgtgetttee 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a
                                                                   231
<210> 460
<211> 231
<212> DNA
<213> Homo sapiens
<400> 460
```

WO 00/04149 PCT/US99/15838

```
gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
 cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
 cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
 gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a
 <210> 461
 <211> 231
 <212> DNA
 <213> Homo sapiens
<400> 461
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcctg tgtgtcctgg 120
gtggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t
<210> 462
<211> 231
<212> DNA
<213> Homo sapiens
<400> 462
aggtaccete attgtageea tgggaaaatt gatgtteagt ggggateagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a
<210> 463
<211> 231
<212> DNA
<213> Homo sapiens
<400> 463
actgagtaga caggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180
tggggaggtg gatcttccag tcgaagcggt atagaagccc gtgtgaaaag c
                                                                231
<210> 464
<211> 231
<212> DNA
<213> Homo sapiens
<400> 464
gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgact 60
aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120
cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c
                                                                231
<210> 465
<211> 231
<212> DNA
<213> Homo sapiens
<400> 465
```

```
catgttgttg tagctgtggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60
gtggcaaatt agcaacaaat totgacatca tatttatggt ttotgtatot ttgttgatga 120
aggatggcac aatttttgct tgtgttcata atatactcag attagttcag ctccatcaga 180
taaactggag acatgcagga cattagggta gtgttgtagc tctggtaatg a
<210> 466
<211> 231
<212> DNA
<213> Homo sapiens
<400> 466
caggtacete titecatigg atacigiget ageaageatg cicleogggg titititaat 60
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaacat ttgcccagga 120
cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180
aataatggag accagtccca caagatgaca accagtcgtt gtgtgcggct g
<210> 467
<211> 311
<212> DNA
<213> Homo sapiens
<400> 467
gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60
tggiggettt teteettttt cateaagaet eeteageagg gageeeagae eageetgeae 120
tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
                                                                 311
ctgcagcaga c
<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens
<400> 468
cattgtgttg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60
aagatetgea tggtgggaag gacetgatga tacagagttt gataggagac aattaaagge 120
tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtggttcaa 240
cgaggacttg gaattgcatg gagctggagc tgaagtttag cccaattgtt tactagttga 300
gtgaatgtgg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360
aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tcactgggtt 420
atttgaagga tgaattgaga taatttattt caggtgccta gaacaatgcc cagattagta 480
catttggtgg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540
gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600
aaattgaact gttaacaaag gaatctctgg tcctgggtaa tggctgagca ccactgagca 660
tttccattcc agttggcttc ttgggtttgc tagctgcatc actagtcatc ttaaataaat 720
gattaaataa agaacttgag aagaacaggt ttcattaaac ataaaatcaa tgtagacgca 840
aattttctgg atgggcaata cttatgttca caggaaatgc tttaaaatat gcagaagata 900
attaaatggc aatggacaaa gtgaaaaact tagacttttt ttttttttt ggaagtatct 960
ggatgttcct tagtcactta aaggagaact gaaaaatagc agtgagttcc acataatcca 1020
acctgtgaga ttaaggctct ttgtggggaa ggacaaagat ctgtaaattt acagtttcct 1080
tccaaagcca acgtcgaatt ttgaaacata tcaaagctct tcttcaagac aaataatcta 1140
tagtacatct ttcttatggg atgcacttat gaaaaatggt ggctgtcaac atctagtcac 1200
```

tttagctctc aaaatggttc attttaagag aaagttttag aatctcatat ttattcctgt 1260 ggaaggacag cattgtggct tggactttat aaggtcttta ttcaactaaa taggtgagaa 1320 ataagaaagg ctgctgactt taccatctga ggccacacat ctgctgaaat ggagataatt 1380 aacatcacta gaaacagcaa gatgacaata taatgtctaa gtagtgacat gtttttgcac 1440 atttccagcc cctttaaata tccacacac caggaagcac aaaaggaagc acagagatcc 1500 ctgggagaaa tgcccggccg ccatcttggg tcatcgatga gcctcgccct gtgcctggtc 1560 ccgcttgtga gggaaggaca ttagaaaatg aattgatgtg ttccttaaag gatgggcagg 1620 aaaacagatc ctgttgtgga tatttatttg aacgggatta cagatttgaa atgaagtcac 1680 aaagtgagca ttaccaatga gaggaaaaca gacgagaaaa tcttgatggc ttcacaagac 1740 atgcaacaaa caaaatggaa tactgtgatg acatgaggca gccaagctgg ggaggagata 1800 accacggggc agagggtcag gattctggcc ctgctgccta aactgtgcgt tcataaccaa 1860 atcatttcat atttctaacc ctcaaaacaa agctgttgta atatctgatc tctacggttc 1920 cttctgggcc caacattctc catatatcca gccacactca tttttaatat ttagttccca 1980 gatetgtact gtgacettte tacaetgtag aataacatta eteatttgt teaaagaeee 2040 ttcgtgttgc tgcctaatat gtagctgact gtttttccta aggagtgttc tggcccaggg 2100 gatetgtgaa caggetggga agcateteaa gatettteea gggttataet taetageaca 2160 cagcatgate attacggagt gaattateta atcaacatea teeteagtgt etttgeecat 2220 actgaaattc atttcccact tttgtgccca ttctcaagac ctcaaaatgt cattccatta 2280 atatcacagg attaactttt ttttttaacc tggaagaatt caatgttaca tgcagctatg 2340 ggaatttaat tacatatttt gttttccagt gcaaagatga ctaagtcctt tatccctccc 2400 ctttgtttga tttttttcc agtataaagt taaaatgctt agccttgtac tgaggctgta 2460 tacagccaca gcctctcccc atccctccag ccttatctgt catcaccatc aacccctccc 2520 atgcacctaa acaaaatcta acttgtaatt ccttgaacat gtcaggcata cattattcct 2580 tctgcctgag aagctcttcc ttgtctctta aatctagaat gatgtaaagt tttgaataag 2640 ttgactatct tacttcatgc aaagaaggga cacatatgag attcatcatc acatgagaca 2700 gcaaatacta aaagtgtaat ttgattataa gagtttagat aaatatatga aatgcaagag 2760 ccacagaggg aatgtttatg gggcacgttt gtaagcctgg gatgtgaagc aaaggcaggg 2820 aacctcatag tatcttatat aatatacttc atttctctat ctctatcaca atatccaaca 2880 agcttttcac agaattcatg cagtgcaaat ccccaaaggt aacctttatc catttcatgg 2940 tgagtgcgct ttagaatttt ggcaaatcat actggtcact tatctcaact ttgagatgtg 3000 tttgtccttg tagttaattg aaagaaatag ggcactcttg tgagccactt tagggttcac 3060 <210> 469 <211> 2229 <212> DNA <213> Homo sapiens <400> 469 agctctttgt aaattcttta ttgccaggag tgaaccctaa agtggctcac aagagtgccc 60 tatttctttc aattaactac aaggacaaac acatctcaaa gttgagataa gtgaccagta 120 tgatttgcca aaattctaaa gcgcactcac catgaaatgg ataaaggtta cctttgggga 180 tttgcactgc atgaattctg tgaaaagctt gttggatatt gtgatagaga tagagaaatg 240 aagtatatta tataagatac tatgaggttc cctgcctttg cttcacatcc caggcttaca 300 aacgtgcccc ataaacattc cctctgtggc tcttgcattt catatattta tctaaactct 360 tataatcaaa tacactttta gtatttgctg tctcatgtga tgatgaatct catatgtgtc 420 ccttctttgc atgaagtaag atagtcaact tattcaaaac tttacatcat tctagattta 480 agagacaagg aagagcttct caggcagaag gaataatgta tgcctgacat gttcaaggaa 540 ttacaagtta gattttgttt aggtgcatgg gaggggttga tggtgatgac agataaggct 600 ggagggatgg ggagaggctg tggctgtata cagcctcagt acaaggctaa gcattttaac 660 tttatactgg aaaaaaatc aaacaaaggg gagggataaa ggacttagtc atctttgcac 720 tggaaaacaa aatatgtaat taaattccca tagctgcatg taacattgaa ttcttccagg 780 ttaaaaaaaa agttaatcct gtgatattaa tggaatgaca ttttgaggtc ttgagaatgg 840 gcacaaaagt gggaaatgaa tttcagtatg ggcaaagaca ctgaggatga tgttgattag 900 ataattcact ccgtaatgat catgctgtgt gctagtaagt ataaccctgg aaagatcttg 960

agatgcttcc cagcctgttc acagatcccc tgggccagaa cactccttag gaaaaacagt 1020 cagctacata ttaggcagca acacgaaggg tctttgaaca aaatgagtaa tgttattcta 1080 cagtgtagaa aggtcacagt acagatctgg gaactaaata ttaaaaaatga gtgtggctgg 1140 atatatggag aatgttgggc ccagaaggaa ccgtagagat cagatattac aacagctttg 1200 ttttqaqqqt taqaaatatg aaatgatttg gttatgaacg cacagtttag gcagcagggc 1260 caqaatcctg accetetgee eegtggttat etecteecea gettggetge eteatgteat 1320 cacagtatic cattitgtit gitgcatgic tigigaagcc atcaagatti tctcgicigi 1380 tttcctctca ttggtaatgc tcactttgtg acttcatttc aaatctgtaa tcccgttcaa 1440 ataaatatcc acaacaggat ctgttttcct gcccatcctt taaggaacac atcaattcat 1500 tttctaatgt ccttccctca caagcgggac caggcacagg gcgaggctca tcgatgaccc 1560 aagatggcgg ccgggcattt ctcccaggga tctctgtgct tccttttgtg cttcctgtgt 1620 gtgtggatat ttaaaggggc tggaaatgtg caaaaacatg tcactactta gacattatat 1680 tgtcatcttg ctgtttctag tgatgttaat tatctccatt tcagcagatg tgtggcctca 1740 gatggtaaag tcagcagcct ttcttatttc tcacctggaa atacatacga ccatttgagg 1800 agacaaatgg caaggtgtca gcataccctg aacttgagtt gagagctaca cacaatatta 1860 ttggtttccg agcatcacaa acaccetete tgtttettea etgggeacag aattttaata 1920 cttatttcag tgggctgttg gcaggaacaa atgaagcaat ctacataaag tcactagtgc 1980 agtgcctgac acacaccatt ctcttgaggt cccctctaga gatcccacag gtcatatgac 2040 ttcttgggga gcagtggctc acacctgtaa tcccagcact ttgggaggct gaggcaggtg 2100 ggtcacctga ggtcaggagt tcaagaccag cctggccaat atggtgaaac cccatctcta 2160 ctaaaaatac aaaaattagc tgggcgtgct ggtgcatgcc tgtaatccca gccccaacac 2220 aatggaatt

<210> 470 <211> 2426

<213> Homo sapiens

<400> 470

<212> DNA

gtaaattett tattgecagg agtgaaceet aaagtggete acaagagtge cetatttett 60 tcaattaact acaaggacaa acacatctca aagttgagat aagtgaccag tatgatttgc 120 caaaattcta aagcgcactc accatgaaat ggataaaggt tacctttggg gatttgcact 180 gcatgaattc tgtgaaaagc ttgttggata ttgtgataga gatagagaaa tgaagtatat 240 tatataagat actatgaggt tecetgeett tgetteacat eecaggetta caaacgtgee 300 ccataaacat tccctctgtg gctcttgcat ttcatatatt tatctaaact cttataatca 360 aattacactt ttagtatttg ctgtctcatg tgatgatgaa tctcatatgt gtcccttctt 420 tgcatgaagt aagatagtca acttattcaa aactttacat cattctagat ttaagagaca 480 aggaagaget teteaggeag aaggaataat gtatgeetga catgtteaag gaattacaag 540 ttagattttg tttaggtgca tgggaggggt tgatggtgat gacagataag gctggaggga 600 tggggagagg ctgtggctgt atacagcctc agtacaaggc taagcatttt aactttatac 660 tggaaaaaaa atcaaacaaa ggggagggat aaaggactta gtcatctttg cactggaaaa 720 caaaatatgt aattaaattc ccatagctgc atgtaacatt gaattcttcc aggttaaaaa 780 aaaaagttaa teetgtgata ttaatggaat gacattttga ggtettgaga atgggeacaa 840 aagtgggaaa tgaatttcag tatgggcaaa gacactgagg atgatgttga ttagataatt 900 cactccgtaa tgatcatgct gtgtgctagt aagtataacc ctggaaagat cttgagatgc 960 ttcccagcct gttcacagat cccctgggcc agaacactcc ttaggaaaaa cagtcagcta 1020 catattaggc agcaacacga agggtctttg aacaaaatga gtaatgttat tctacagtgt 1080 agaaaggtca cagtacagat ctgggaacta aatattaaaa atgagtgtgg ctggatatat 1140 ggagaatgtt gggcccagaa ggaaccgtag agatcagata ttacaacagc tttgttttga 1200 gggttagaaa tatgaaatga titggttatg aacgcacagt ttaggcagca gggccagaat 1260 cetgacecte tgeceegtgg ttatetecte eccagettgg etgeeteatg teateaeagt 1320 attccatttt gtttgttgca tgtcttgtga agccatcaag attttctcgt ctgttttcct 1380 ctcattggta atgctcactt tgtgacttca tttcaaatct gtaatcccgt tcaaataaat 1440 atccacaaca ggatctgttt tcctgcccat cctttaagga acacatcaat tcattttcta 1500 atgtccttcc ctcacaagcg ggaccaggca cagggcgagg ctcatcgatg acccaagatg 1560

WO 00/04149 PCT/US99/15838

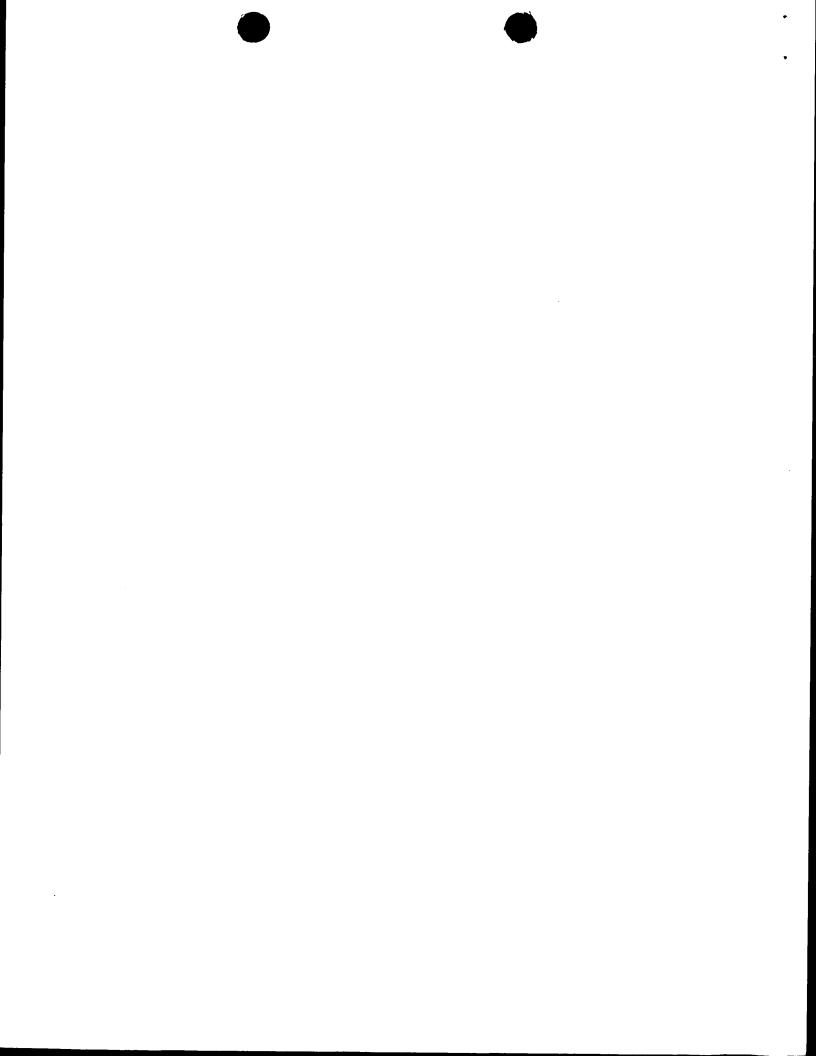
```
gcggccgggc atttctccca gggatctctg tgcttccttt tgtgcttcct gtgtgtgtgg 1620
 atatttaaag gggctggaaa tgtgcaaaaa catgtcacta cttagacatt atattgtcat 1680
 cttgctgttt ctagtgatgt taattatctc catttcagca gatgtgtggc ctcagatggt 1740
 aaagtcagca gcctttctta tttctcacct ggaaatacat acgaccattt gaggagacaa 1800
 atggcaaggt gtcagcatac cctgaacttg agttgagagc tacacacaat attattggtt 1860
 teegageate acaaacacee tetetgttte tteaetggge acagaatttt aataettatt 1920
 tcagtgggct gttggcagga acaaatgaag caatctacat aaagtcacta gtgcagtgcc 1980
 tgacacacac cattetettg aggteeette tagagateee acaggteata tgacttettg 2040
 gggagcagtg gctcacacct gtaatcccag cactttggga ggctgaggca ggtgggtcac 2100
 ctgaggtcag gagttcaaga ccagcctggc caatatggtg aaaccccatc tctactaaaa 2160
atacaaaaat tagctgggcg tgctggtgca tgcctgtaat cccagctact tgggaggctg 2220
aggcaggaga attgctggaa catgggaggc ggaggttgca gtgagctgta attgtgccat 2280
tgcactcgaa cctgggcgac agagtggaac tctgtttcca aaaaaacaaac aaacaaaaa 2340
ggcatagtca gatacaacgt gggtgggatg tgtaaataga agcaggatat aaagggcatg 2400
 gggtgacggt tttgcccaac acaatg
<210> 471
 <211> 812
 <212> DNA
<213> Homo sapiens
<400> 471
gaacaaaatg agtaatgtta ttctacagtg tagaaaggtc acagtacaga tctgggaact 60
aaatattaaa aatgagtgtg gctggatata tggagaatgt tgggcccaga aggaaccgta 120
gagatcagat attacaacag ctttgttttg agggttagaa atatgaaatg atttggttat 180
gaacgcacag tttaggcagc agggccagaa tcctgaccct ctgccccgtg gttatctcct 240
ccccagcttg gctgcctcat gtcatcacag tattccattt tgtttgttgc atgtcttgtg 300
aagccatcaa gattttctcg tctgttttcc tctcattggt aatgctcact ttgtgacttc 360
atttcaaatc tgtaatcccg ttcaaataaa tatccacaac aggatctgtt ttcctgccca 420
teetttaagg aacacateaa tteattttet aatgteette eetcacaage gggaccagge 480
acagggcgag gctcatcgat gacccaagat ggcggccggg cattteteec agggatetet 540
gtgcttcctt ttgtgcttcc tgtgtgtgtg gatatttaaa ggggctggaa atgtgcaaaa 600
acatgtcact acttagacat tatattgtca tcttgctgtt tctagtgatg ttaattatct 660
ccatttcagc agatgtgtgg cctcagatgg taaagtcagc agcctttctt atttctcacc 720
tetgtateat caggteette ecaccatgea gatetteetg gteteeeteg getgeageea 780
cacaaatctc ccctctgttt ttctgatgcc ag
<210> 472
<211> 515
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(515)
<223> n = A,T,C or G
<400> 472
acggagactt attttctgat attgtctgca tatgtatgtt tttaagagtc tggaaatagt 60
cttatgactt tcctatcatg cttattaata aataatacag cccagagaag atgaaaatgg 120
gttccagaat tattggtcct tgcagcccgg tgaatctcag caagaggaac caccaactga 180
caatcaggat attgaacctg gacaagagag agaaggaaca cctccgatcg aagaacgtaa 240
agtagaaggt gattgccagg aaatggatct ggaaaagact cggagtgagc gtggagatgg 300
ctctgatgta aaagagaaga ctccacctaa tcctaagcat gctaagacta aagaagcagg 360
agatgggcag ccataagtta aaaagaagac aagctgaagc tacacacatg gctgatgtca 420
```



PCT/US99/15838 -

169

cattgaaaat gtgactgaaa atttgaaaat tctctcaata aagtttgagt tttctctgaa 480 gaaaaaaaaa naaaaaaaa aaanaaaaan aaaaa 515









INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7: C12N 15/12, C07K 14/47, C12Q 1/68, A61K 39/395, G01N 33/68, 33/574, C07K 16/30, C12N 15/62, 5/02 // A61P 35/00

A3

(11) International Publication Number:

WO 00/04149

(43) International Publication Date:

27 January 2000 (27.01.00)

(21) International Application Number:

PCT/US99/15838

(22) International Filing Date:

14 July 1999 (14.07.99)

(30) Priority Data:

illity Data.		
09/115,453	14 July 1998 (14.07.98)	US
09/116,134	14 July 1998 (14.07.98)	US
09/159,822	23 September 1998 (23.09.98)	US
09/159,812	23 September 1998 (23.09.98)	US
09/232,880	15 January 1999 (15.01.99)	US
09/232,149	15 January 1999 (15.01.99)	US
09/288,946	9 April 1999 (09.04.99)	US
	•	

- (71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).
- (72) Inventors: DILLON, Davin, Clifford; 21607 N.E. 24th Street, Redmond, WA 98053 (US). HARLOCKER, Susan, Louise; 6203 20th Avenue N.W., Seattle, WA 98107 (US). YUQIU, Jiang; 5001 South 232nd Street, Kent, WA 98032 (US). XU, Jiangchun; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). MITCHAM, Jennifer, Lynn; 16677 Northeast 88th Street, Redmond, WA 98052 (US).

(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

(88) Date of publication of the international search report: 20 July 2000 (20.07.00)

(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
ΑT	Austria	FR	France	LU	Luxembourg	SN	
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Senegal
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Swaziland Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Togo
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Tajikistan
BF	Burkina Faso	GR	Greece	.,,,,,	Republic of Macedonia	TR	Turkmenistan
BG	Bulgaria	HU	Hungary	ML	Mali		Turkey
BJ	Benin	IE	Ireland	MN	Mongolia	TT	Trinidad and Tobago
BR	Brazil	IL	Israel	MR	Mauritania	UA	Ukraine
BY	Belarus	IS	Iceland	MW	Malawi	UG	Uganda
CA	Canada	IT	Italy	MX	Maiawi Mexico	US	United States of America
CF	Central African Republic	JP	Japan	NE.		UZ	Uzbekistan
CG	Congo	KE	Kenya		Niger	VN	Viet Nam
СН	Switzerland	KG	Kyrgyzstan	NL NO	Netherlands	YU	Yugoslavia
CI	Côte d'Ivoire	KP	Democratic People's	_	Norway	ZW	Zimbabwe
CM	Cameroon	141	Republic of Korea	NZ	New Zealand		
CN	China	KR	Republic of Korea	PL PT	Poland		
CU	Cuba	KZ	Kazakstan		Portugal		
CZ	Czech Republic	LC	Saint Lucia	RO	Romania		
DE	Germany	LI	Liechtenstein	RU	Russian Federation		
DK	Denmark			SD	Sudan		
EE	Estonia	LK	Sri Lanka	SE	Sweden		
1515	Catolita	LR	Liberia	SG	Singapore		
						•	

lication No PCT/US 99/15838

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/12 C07K14/47

C12Q1/68 C12N15/62 A61K39/395 C12N5/02

G01N33/68

//A61P35/00

C07K16/30 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS	CONSIDERED	10 BE HELEVANI

33909 A (CORIXA CORP) tember 1997 (1997-09-18) ole document N H O: "Therapeutic immunization t cancer antigens using genetically	1-22, 29-31, 35-49, 53-79
 N H O: "Therapeutic immunization	
	l
red cells" TECHNOLOGY, , no. 3, ber 1997 (1997-10-01), pages 2, XP004097000 1380-2933 ole document	23-28, 32-34, 53-57
-/	
2	2, XP004097000 1380-2933

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.			
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family			
Date of the actual completion of the international search	Date of mailing of the international search report			
31 January 2000	0 4. 05. 00			
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer ANDRES S.M.			

Form PCT/ISA/210 (second sheet) (July 1992)

INTERMATIONAL SEARCH REPORT

rional Application No PCT, US 99/15838

C.(Continua	ntion) DOCUMENTS CONSIDERED TO BE RELEVANT	·
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Α	CHU R S ET AL: "CPG OLIGODEOXYNUCLEOTIDES ACT AS ADJUVANTS THAT SWITCH ON T HELPER 1 (TH1) IMMUNITY" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 186, no. 10, 1 November 1997 (1997-11-01), pages 1623-1631, XP002910130 ISSN: 0022-1007 the whole document	14-20, 25-27, 41-47
A	EP 0 317 141 A (BECTON DICKINSON CO) 24 May 1989 (1989-05-24) the whole document	50-52
Α	ZITVOGEL L ET AL: "Eradication of established murine tumors using a novel cell-free vaccine: dendritic cell-derived exosomes" NATURE MEDICINE, vol. 4, no. 5, 1 May 1998 (1998-05-01), pages 594-600, XP002085387 ISSN: 1078-8956 cited in the application	·
P,X	WO 98 37093 A (CORIXA CORP) 27 August 1998 (1998-08-27)	1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79
	page 3, line 20 -page 22, line 2 page 35, line 9 - last line page 76, line 34 -page 78, line 22 claims	
P,X	WO 98 37418 A (CORIXA CORP) 27 August 1998 (1998-08-27)	1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79
	page 2 -page 24 example 2 page 35, line 15 -page 36, line 11 page 81, line 14 -page 83, line 11 claims	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)



In application No.
PCT/US 99/ 15838

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claims 29-34, 48-49, 52, 55-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. Claims Nos.:
3.	because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
	rnational Searching Authority found multiple inventions in this international application, as follows:
	e additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
•	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is estricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark o	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 1. Claims: 1-79 (all partially)

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

Inventions 2. to 439. Claims: 1-79 (all partially and as far as applicable)

As for subject 1. but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328,330,332-335,340-375,381,382 and 384-472.

INTERNATION L SEARCH REPORT

mation of the ent family members

PC1, JS 29/15838

Patent document cited in search report		Publication date		atent family member(s)	Publication date
WO 9733909	А	18-09-1997	AU BR CA EP NO US	2329597 A 9708082 A 2249742 A 0914335 A 984229 A 6034218 A	01-10-1997 27-07-1999 18-09-1997 12-05-1999 13-11-1998 07-03-2000
EP 0317141	A	24-05-1989	US AT DE DE ES JP	5041289 A 108659 T 3850745 D 3850745 T 2059537 T 2002345 A	20-08-1991 15-08-1994 25-08-1994 24-11-1994 16-11-1994 08-01-1990
WO 9837093	Α	27-08-1998	AU NO ZA	6181898 A 994069 A 9801585 A	09-09-1998 22-10-1999 04-09-1998
WO 9837418	A	27-08-1998	AU EP ZA	6536898 A 0972201 A 9801536 A	09-09-1998 19-01-2000 08-01-1999

Form PCT/ISA/210 (patent family annex) (July 1992)

